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Addendum 2
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Health Effects Models for Nuclear Power Plant Accident Consequence Analysis

Modification of Models Resulting From Addition of Effects of Exposure to Alpha-Emitting Radionuclides

Part II: Scientific Bases for Health Effects Models

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Prepared for
U.S. Nuclear Regulatory Commission

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Part II: Scientific Bases for Health Effects Models

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FOREWORD

The Nuclear Regulatory Commission (NRC) has sponsored several studies to identify and quantify, through the use of models, the potential health effects of accidental releases of radionuclides from nuclear power plants. The Reactor Safety Study (WASH-1400, Appendix VI) provided the basis for most of the earlier estimates related to these health effects. Subsequent efforts by NRC-supported groups resulted in improved health effects models that were published in report entitled "Health Effects Models for Nuclear Power Plant Consequence Analysis", NUREG/CR-4214, 1985 and revised further in the 1989 report NUREG/CR-4214, Rev. 1, Part II. The health effects models presented in the 1989 NUREG/CR-4214 report were developed for exposure to low-linear energy transfer (LET) (beta and gamma) radiation based on the best scientific information available at that time. Since the 1989 report was published, two addenda to that report have been prepared to 1) incorporate other scientific information related to low-LET health effects models and 2) extend the models to consider the possible health consequences of the addition of alpha-emitting radionuclides to the exposure source term.

The first addendum report, entitled "Health Effects Models for Nuclear Power Plant Accident Consequence Analysis, Modifications of Models Resulting from Recent Reports on Health Effects of Ionizing Radiation, Low LET Radiation, Part II: Scientific Bases for Health Effects Models," was published in 1991 as NUREG/CR-4214, Rev. 1, Part II, Addendum 1.

This second addendum addresses the possibility that some fraction of the accident source term from an operating nuclear power plant comprises alpha-emitting radionuclides. Consideration of chronic high-LET exposure from alpha radiation as well as acute and chronic exposure to low-LET beta and gamma radiations is a reasonable extension of the health effects model. All nuclear power plants contain alpha-emitting radionuclides in their fuel inventory, so the possibility exists for combined exposure to beta, gamma and alpha radiations in the event of an accidental release. While the alpha-emitting fraction of radionuclides in the fuel inventory could be important, it is usually quite small.

The NRC staff believes that the health effects models and risk coefficients presented in NUREG/CR-4214, Rev. 1, Part II and its addenda, constitute "state-of-the-art" and are useful in performance of risk assessment analyses. However, NUREG/CR-4214, Rev. 1, Part II, Addendum 2 is not a substitute for NRC regulations, and compliance is not required. The approaches and/or methods described in this NUREG are provided for information only. Publication of this report does not necessarily constitute NRC approval of agreement with the information contained herein.

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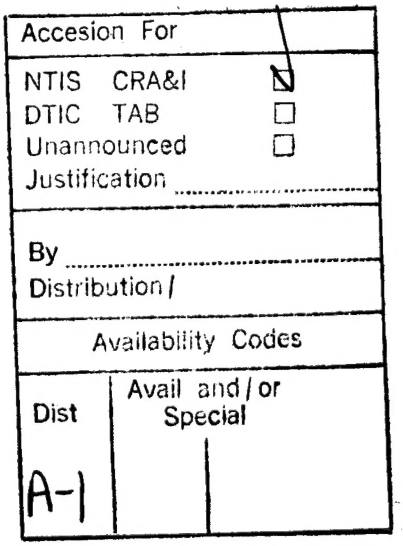
ABSTRACT

Several studies designed to identify and quantify the potential health effects of accidental releases of radionuclides from nuclear power plants have been sponsored by the Nuclear Regulatory Commission. Report NUREG/CR-4214, Rev. 1, Part II (NRC, 1989a) describes in detail the most recent health effects models that have evolved from these efforts. Since the Part II report was published in 1989, two addenda to that report have been prepared to 1) incorporate other scientific information related to low-LET health effects models and 2) extend the models to consider the possible health consequences of including alpha-emitting actinide radionuclides in the exposure source term. The first addendum was published as NUREG/CR-4214, Rev. 1, Part II, Addendum 1 (NRC, 1991). This report, the second addendum to the Part II report, extends the health effects models to consider chronic irradiation from alpha-emitting radionuclides as well as low-LET sources. Consistent with the organization of past reports, this report has three main sections that address early-occurring and continuing effects, late somatic effects, and genetic effects. These results should be used with the basic NUREG/CR-4214 report and Addendum 1 to obtain current views on potential health effects models for radionuclides released accidentally from nuclear power plants.



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EXECUTIVE SUMMARY

The Nuclear Regulatory Commission has sponsored several studies to identify and quantify, through use of health effects models, the potential health effects of accidental releases of radionuclides from nuclear power plants. Included in these efforts have been the health effects estimates in the Reactor Safety Study (NRC, 1975), and the improved models given in report NUREG/CR-4214 (NRC, 1985) and revised further in report NUREG/CR-4214, Rev. 1, Part II (NRC, 1989a). The 1989 report was developed for exposure to low-LET (beta and gamma) radiation based on the best scientific information available at that time. Since the 1989 report was published, two addenda to that report have been prepared to 1) incorporate other scientific information related to low-LET health effects models, and 2) extend the models to consider the possible health consequences of the addition of alpha-emitting radionuclides to the exposure source term.

The first addendum report, entitled "Health Effects Models for Nuclear Power Plant Accident Consequence Analysis, Modifications of Models Resulting from Recent Reports on Health Effects of Ionizing Radiation, Low-LET Radiation, Part II: Scientific Bases for Health Effects Models" was published as NUREG/CR-4214, Rev. 1, Part II, Addendum 1 (NRC, 1991). Several major health effects reports that were published recently, which could impact the health effects models presented in NUREG/CR-4214 (NRC, 1989a), were reviewed in that report. Included in this review were the 1986 and 1988 reports by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 1986; 1988), the National Academy of Sciences/National Research Council BEIR V Committee Report (NAS/NRC, 1990), and Publication 60 of the International Commission on Radiological Protection (ICRP, 1991).

This report, the second addendum, is directed to the possibility that some fraction of the exposure source term from an operating nuclear power plant comprises alpha-emitting radionuclides. Consideration is given to both chronic alpha irradiation and acute and chronic low-LET irradiation. This is a reasonable extension of the health effects model recognizing that all nuclear power plants contain some alpha-emitting actinide radionuclides in their fuel inventory and the possibility exists for an accident to produce some combined exposure to low- and high-LET radiations.

Exposure to these alpha-emitting radionuclides can occur by inhalation, ingestion, or through cuts or wounds. For the purposes of this report, inhalation is considered to be the major route of exposure. Consideration of various radionuclides of interest is directed primarily to isotopes of plutonium, americium and curium. As was done in Addendum 1 (NRC, 1991), this report also addresses the three main topics of the main NUREG/CR-4214 report (NRC, 1989a): early-occurring and continuing effects, late somatic effects, and genetic effects.

Early-Occurring and Continuing Effects

Existing data on early-occurring and continuing deterministic effects based on studies in humans and laboratory animals were reviewed. Historically, very few accidental human exposures have involved inhalation of transuranic alpha-emitting radionuclides at levels where deterministic effects would be expected. Studies of laboratory animals that inhaled large quantities of alpha-emitting radionuclides have provided much of what we know about the deterministic effects resulting from large radiation doses from such sources.

The primary early-occurring and continuing effects seen after inhalation of large amounts of an alpha-emitting radionuclide are radiation pneumonitis and pulmonary fibrosis. Studies of the effectiveness of chronic alpha irradiation compared to chronic beta irradiation in terms of producing these effects in laboratory animals indicate that a value of 7 should be used as a central estimate for the relative biological effectiveness (RBE) of alpha to beta radiations. Upper and lower bounds of 10 and 5, respectively, reflect observed variability in the experimentally determined RBE values.

The NUREG/CR-4214 model (NRC, 1989a) was used for purposes of these assessments. Each deterministic effect of interest is modeled using the Weibull dose-response function evaluated with a normalized dose, X, where for low-LET radiation $X=1$ corresponds to an LD_{50} or ED_{50} absorbed dose regardless of the dose-rate pattern. To account for the possible effects of a changing dose-rate pattern, increments of X can be used over different time intervals and then added to obtain the total X.

The recommended approach for computing the lethality or morbidity hazard and corresponding risk for a combined exposure that includes both low-LET beta and gamma radiations and high-LET alpha radiation is to: a) multiply the absorbed alpha radiation dose rate by the RBE for deterministic effects in the organ considered (use RBE=7 for the lung); b) add the product obtained to the low-LET dose rate; c) calculate the normalized dose in the same way as is done for low-LET radiation; and d) use the total normalized dose to compute the hazard and risk for the deterministic effect considered. To make these computations, a preferred value of 7 is recommended for the shape parameter in the Weibull model for early-occurring and continuing effects of combined (simultaneous) exposure of the lung to alpha, beta, and gamma radiations.

Model parameters for pulmonary deaths from deterministic effects in children or adults age 40 or less are given in Table 2.4 (p. 19) along with estimated values for the upper and lower bounds for these parameters. This table has been adapted from Table 2.14 in the NUREG/CR-4214 report (NRC, 1989a). For individuals over age 40, the listed D_{50} and threshold estimates should be reduced by a factor of 2.

Late Somatic Effects

Assuming that inhalation is the primary pathway of exposure to consider for this report, it is concluded that the critical targets for late somatic effects of alpha radiation are the lung, liver, and bone. For each of these organs, available data from human populations and life-span studies in laboratory animals are reviewed and a central estimate of risk is given. For the purposes of incorporation of these risk estimates into the NUREG/CR-4214 models (NRC, 1989a), it is recommended that the high- and low-LET, radiation-associated risks be evaluated separately and then added.

The low-LET contribution to the overall risk for a specific type of cancer should be evaluated using the models in Addendum 1 (NRC, 1991). These are reproduced here as Tables 3.2 and 3.3 (pp. 44, 45) for the convenience of the user. In like manner, Table 3.4 (p. 47) reproduces the central, upper, and lower lifetime risk estimates for mortality from exposure to low-LET radiation, as originally published in Table 3.22 of Addendum 1.

The central estimate of risk of lung cancer from inhalation of alpha-emitting radionuclides was estimated by multiplying the central estimate for lung cancer (given for low-LET in Table 3.3) by an RBE for chronic alpha radiation vs. chronic beta radiation of 20. This resulted in a rounded central estimate of 1600 lung cancers per 10^4 person-Gy. This estimate is consistent with the results of a review of available data on the observed risks of lung cancer in uranium miners exposed to radon and radon progeny, and of lung cancer in various species of laboratory animals that inhaled different alpha-emitting radionuclides.

For liver cancer, a central lifetime risk estimate of 300 cancers per 10^4 person-Gy is recommended. This estimate is based on currently available data from the long-term followup of persons who received an intravenous injection of the radiographic contrast medium, Thorotrast. For bone cancer induced by alpha radiation, a factor of 12 bone cancers per 10^4 person-Gy was selected based on currently available data from adults who received single or multiple injections of ^{224}Ra. This risk factor is based on the dose to endosteal bone surfaces.

These risk estimates are listed in Table 3.5 (p. 49) along with recommended values for upper and lower bounds that reflect uncertainties in the DDREF for low-LET radiation, the RBE for chronic alpha vs. beta radiation, and other factors similar to those considered in evaluating uncertainties in effects of low-LET exposure.

Genetic Effects

Estimates are made of numbers of genetic effects that may occur following gonadal exposures of human populations by alpha radiation from radionuclides released as a consequence of a nuclear reactor accident. These estimates are based on BEIR IV recommendations for RBE factors to convert estimates of genetic effects from low dose-rate, low-LET exposures to estimates for internally incorporated alpha-emitting radionuclides. Using an RBE of 2.5 for all mutations and 15 for unbalanced translocations the numbers of genetic effects that might occur as a consequence of a nuclear power plant accident were estimated for the various classes. Table 4.1 (p. 56), which summarizes the results of these estimates of genetic effects for both alpha and low-LET radiations, is adapted from Table 4.1 in Addendum 1 (NRC, 1991). Also, Table 4.2 from Addendum 1, which provides genetic risk estimates for selected irregularly inherited diseases except for congenital anomalies, is expanded as Table 4.2 (p. 58) in this report to consider both chronic low-LET and high-LET radiations.

ACKNOWLEDGEMENTS

As was true for the underlying report for which this report is an addendum, NUREG/CR-4214, Rev. 1, Part II (NRC, 1989a), a number of authors have contributed sections. Because of the direct connection between this addendum and the 1989 NUREG report, it was fortunate that the authors of this addendum were authors or co-authors of the respective chapters in the 1989 report. These authors were Dr. Bobby Scott, Inhalation Toxicology Research Institute; Dr. Ethel Gilbert, Battelle Pacific Northwest Laboratory; Dr. Seymour Abrahamson, University of Wisconsin; and Dr. Michael Bender, Brookhaven National Laboratory. Dr. Bruce Boecker, Inhalation Toxicology Research Institute, also a co-author, coordinated this effort.

Beginning with the preparation of the original NUREG/CR-4214 report in 1985 and continuing during the preparation of the 1989 revised NUREG/CR-4214 report, an Advisory Committee has provided valuable input. To carry forward the quality and consistency of these reports to this addendum, a number of members of the Advisory Committee served as authors or reviewers of this addendum:

Seymour Abrahamson, Ph.D.	University of Wisconsin
William J. Bair, Ph.D.	Battelle Pacific Northwest Laboratories
Michael A Bender, Ph.D.	Brookhaven National Laboratory
Bruce B. Boecker, Ph.D.	Inhalation Toxicology Research Institute
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Eugene L. Saenger, M.D.	University of Cincinnati College of Medicine
Warren K. Sinclair, Ph.D.	National Council on Radiation Protection and Measurements
Niel Wald, M.D.	University of Pittsburgh
Shlomo Yaniv, Sc.D.	U.S. Nuclear Regulatory Commission

Other expert reviews were provided by Dr. Carter Denniston, University of Wisconsin; Dr. Fletcher Hahn, Inhalation Toxicology Research Institute; Dr. David Chanin, Sandia National Laboratories; and Drs. Jerry Puskin and Neal Nelson, U.S. Environmental Protection Agency.

Every effort has been expended to respond to the comments of all these reviewers. Recognizing that such an extensive review process can, at times, generate diverging opinions on certain points, the authors have used their best scientific judgement in preparing the final version of this report.

The authors are also pleased to acknowledge the diligent and tireless efforts of Ms. Mary G. Campos in the preparation and publication of Addendums 1 and 2 to NUREG/CR-4214. Her production skills and careful attention to multitudinous details have been invaluable ingredients of this overall process.

1.0 INTRODUCTION

1.1 Background

The Nuclear Regulatory Commission (NRC) has sponsored several studies to identify and quantify, through use of models, the potential health effects of accidental releases of radionuclides from nuclear power plants. The Reactor Safety Study (NRC, 1975) provided the basis for most of the earlier official estimates related to these health effects. Subsequent efforts by NRC-supported groups resulted in improved health effects models that were published in report NUREG/CR-4214 (NRC, 1985) and revised further in report NUREG/CR-4214, Rev. 1, Part II (NRC, 1989a). The health effects models presented in the 1989 NUREG/CR-4214 report were developed for exposure to low-linear energy transfer (LET) (beta and gamma) radiation based on the best scientific information available at that time. Since the 1989 report was published, two addenda to that report have been prepared to 1) incorporate other scientific information related to low-LET health effects models and 2) extend the models to consider the possible health consequences of the addition of alpha-emitting radionuclides to the exposure source term.

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This second addendum addresses the possibility that some fraction of the accident source term from an operating nuclear power plant comprises alpha-emitting radionuclides. Consideration of chronic high-LET exposure from alpha radiation as well as acute and chronic exposure to low-LET beta and gamma radiations is a reasonable extension of the health effects model. All nuclear power plants contain some alpha-emitting radionuclides in their fuel inventory, so the possibility exists for combined exposure to beta, gamma and alpha radiations in the event of an accidental release. While the alpha-emitting fraction of radionuclides in the fuel inventory could be important, it is usually quite small as indicated below.

Alpert *et al.* (1986) studied the relative importance to offsite health and economic consequences of radionuclides in a nuclear reactor core assuming that an equal fraction of the inventory of each radionuclide was released. These calculations, made using the SANDIA-ORIGEN code, identified 60

nuclides of 25 elements that could be important for offsite consequence analysis of nuclear power plant accidents in the U.S. Factors considered in this selection included the inventory, half-life, and potential biological hazard of each radionuclide. The relative radiological importance of those elements/nuclides that could contribute to offsite consequences were then determined using the MACCS code (NRC, 1990b). Table 1.1 lists the radionuclides and lung clearance classes used in MACCS. The relative values obtained by such calculations were then scaled by the release fractions specified for a particular release scenario called SST1 (Aldrich and Sprung, 1982) to obtain an indication of the potential importance of various elements/nuclides in producing early- or late-occurring health effects. These calculations showed that alpha-emitting radionuclides of elements such as Pu, Am, and Cm can contribute to both the early- and late-occurring health effects that might result from a nuclear reactor accident.

Table 1.1

List of radionuclides and lung clearance classes as used in the MACCS code[a]

Nuclide	Lung clearance class	Nuclide	Lung clearance class	Nuclide	Lung clearance class
Co-58	years	Ru-103	years	Cs-136	days
Co-60	years	Ru-105	years	Cs-137	days
Kr-85	inert gas	Ru-106	years	Ba-139	days
Kr-85m	inert gas	Rh-105	years	Ba-140	days
Kr-87	inert gas	Sb-127	weeks	La-140	weeks
Kr-88	inert gas	Sb-129	weeks	La-141	weeks
Rb-86	days	Te-127	weeks	La-142	weeks
Sr-89	days	Te-127m	weeks	Ce-141	years
Sr-90	days	Te-129	weeks	Ce-143	years
Sr-91	days	Te-129m	weeks	Ce-144	years
Sr-92	days	Te-131m	weeks	Pr-143	years
Y-90	years	Te-132	weeks	Nd-147	years
Y-91	years	I-131	days	Np-239	weeks
Y-92	years	I-132	days	Pu-238[b]	years
Y-93	years	I-133	days	Pu-239[b]	years
Zr-95	weeks	I-134	days	Pu-240[b]	years
Zr-97	weeks	I-135	days	Pu-241	years
Nb-95	years	Xe-133	gas	Am-241[b]	weeks
Mo-99	years	Xe-135	gas	Cm-242[b]	weeks
Tc-99M	weeks	Cs-134	days	Cm-244[b]	weeks

[a] From (NRC, 1990b)

[b] Alpha-emitting radionuclide

Studies show that some victims of the Chernobyl accident inhaled small amounts of alpha-emitting radionuclides. Following the accident, soil samples taken within the 30-km zone were examined for their content of alpha-emitting transuranic elements. The total activity concentrations of the samples ranged from 2 to 2000 Bq/g (USSR, 1986). Soil samples from the 1.5-km zone were also examined. Results for one southwestern site (road surface at 1.5 km from the reactor) are given in Table 1.2. These results demonstrate that alpha activity represented 0.11% of the total quantity of radioactive material present. Air samples analyzed for the contents of ^{238}Pu, ^{239}Pu, ^{240}Pu, and ^{242}Cm relative to ^{144}Ce (i.e., alpha activity/cerium beta activity) produced ratios in the range 0.00029 to 0.0087.

Table 1.2

Composition of radionuclides in soil samples taken on May 8, 1986, at a distance of 1.5 km from the Chernobyl reactor (USSR, 1986)

Nuclide	Specific activity (10^5 Bq/g)	Percentage of total activity
^{95}Zr	36.0	30.9
^{103}Ru	1.7	1.5
^{131}I	6.3	5.4
^{140}Ba	21.0	18.0
^{141}Ce	28.0	24.0
^{144}Ce	17.0	14.6
^{239}Np	6.4	5.5
Alpha-emitting radionuclides	0.13	0.1

Analyses were made for transuranic elements in urine specimens from 266 victims, primarily plant personnel and auxiliary staff (635 analyses) of the Chernobyl accident (UNSCEAR, 1988). In some cases, analyses were conducted before and after administration of the chelating agent CaDTPA, a calcium salt of diethylenetriaminepentaacetic acid. Negative results for alpha activity in the urine, as well as negative results after chelation treatment, demonstrated the absence of significant plutonium contamination of any patients. Post-mortem alpha spectrometry tests showed the presence of transuranics was confined to the lung. The activity per lung ranged from 74 to 399 Bq. Curium accounted for up to 90% of the alpha activity; plutonium and americium together accounted for about 10%.

1.2 Modes of Exposure to Alpha Radiation

For the accidental release scenarios of interest for nuclear power plants, the possible exposure modes include inhalation, ingestion, and deposition on the external surfaces of the body. These exposure modes have different degrees of importance because of the physical and chemical properties of actinide radionuclides and their alpha-particle emissions.

Inhalation is the major route of exposure to alpha-emitting radionuclides that can lead to biological effects. When inhaled, alpha-emitting radionuclides, like other inhaled materials, are deposited at different locations along the respiratory tract. The aerodynamic particle size distribution of the exposure aerosol plays a major role in determining how much aerosol is likely to be inspired per breath, how much of this inspired aerosol may deposit in the respiratory tract, and in what region it is likely to deposit.

Relatively insoluble forms of these radionuclides if inhaled and deposited in the respiratory tract may be retained in the pulmonary region for prolonged times. Clearance of deposited particles occurs by mucociliary activity up the trachea followed by swallowing and excretion in the feces, or by clearance to the regional lymph nodes associated with the respiratory tract. Also, these particles may be dissolved and the radionuclide absorbed into the bloodstream. For relatively insoluble radionuclides, the respiratory tract is the major organ system irradiated. The local distribution of alpha radiation dose in the lung will depend on the energies of emitted alpha radiations, the rate of radioactive decay, the size and activity distribution of inhaled carrier particles, and factors influencing changes in local activity over time. Factors that may influence changes in local deposits of radionuclides include carrier particle solubility and the rate of mechanical clearance from the lung.

Dissolution of the inhaled particles will occur at rates dependent on their physical and chemical properties. After dissolution, the radionuclide may be absorbed into the systemic circulation and translocated to other major organ sites such as the skeleton or liver where it may be retained with a very long biological half-life. Thus, for relatively soluble radionuclides, other organs may receive absorbed doses that equal or exceed the dose received by the lung.

There is a broad range of biological half-lives, T_B, associated with different radionuclides in different chemical compounds and forms. For radiation protection purposes, the ICRP has established three classes of radionuclides and forms, based on their retention in the lung (ICRP, 1979). These classes and their representative T_B values are: D (days) with T_B=0.5 d, W (weeks) with T_B=50 d, and Y (years) with T_B=500 d. The degree to which other organs beyond the lung are irradiated is inversely related to the magnitude of the effective half-life for radionuclide retention which accounts for reductions due to biological clearance processes and radioactive decay.

Ingestion is not considered to be an exposure route of major importance for the production of early-occurring deterministic effects. Because of the relatively insoluble nature of transuranic radionuclides in the gastrointestinal tract, the fraction of ingested material absorbed in the early post-exposure period is minimal. Also, the risk of deterministic effects occurring in the gastrointestinal tract due to direct alpha irradiation from radionuclides passing through with the other gastrointestinal

contents is thought to be negligible because the short-ranged alpha particles are absorbed in the contents or are unlikely to penetrate the mucous layer covering the tract. The relative importance of the ingestion route for late-occurring somatic effects will depend on the balance between the magnitude and duration of such an exposure and the relatively low rate of absorption because of the insoluble nature of actinides in the gastrointestinal tract.

Direct radiation effects from alpha-emitting radionuclides deposited on intact skin are unlikely because the short range of the alpha radiation does not allow them to penetrate and produce skin burns. In the event of disruption of the skin surface by burns or cuts, it is possible that a small fraction of the deposited radionuclide may become embedded subcutaneously. Again, such an occurrence should result in minimal local damage because of the short range of alpha emissions in solid tissues (~ 40 μm), but some long-term absorption into the systemic circulation could lead to translocation and deposition in internal organs such as the liver or skeleton.

Alpha-emitting radionuclides deposited on the exterior portion of the eye are unlikely to cause significant deterministic effects. Radionuclides emitting sufficiently energetic alpha particles, >5 MeV, could deposit energy in the cornea that could result in minor local damage. The induction of cataracts from externally deposited, alpha-emitting radionuclides is unlikely because of the short range of the alpha particles.

Because of the importance of the inhalation route as a mode of exposure to alpha-emitting radionuclides released from an accident at a nuclear power plant, the radiobiological consequences of such an exposure are explored in greater detail in the following chapters. As was done in Addendum 1, this report addresses the three main topics of the NUREG/CR-4214 (NRC, 1989a) report: early-occurring and continuing effects, late somatic effects, and genetic effects.

2.0 EARLY-OCCURRING AND CONTINUING EFFECTS

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2.1 Introduction

As demonstrated in the nuclear power plant accident at Chernobyl, individuals at such an accident site can receive large doses of external radiation and also internal doses arising from inhalation of complex mixtures of radionuclides. Large radiation doses can cause early-occurring and continuing deterministic effects, as well as late-occurring stochastic effects.[a]

Examples of early-occurring deterministic effects include the classical prodromal symptoms (e.g., vomiting, diarrhea), death from injury to the bone marrow (hematopoietic death), death from injury to the gastrointestinal tract (gastrointestinal death), and death from injury to the lung (pulmonary death) (Yaniv and Scott, 1990). These early deterministic effects occur within days to weeks after exposure. Continuing deterministic effects, such as hypothyroidism, pulmonary fibrosis, and cataracts, may develop over a longer period of time and continue for years. Effects resulting from irradiation of pregnant women during a nuclear accident may include increased cases of embryo loss, malformation, fetal death, and mentally retarded children.

Dose-response relationships for deterministic effects vary for different tissues and depend on covariates that include dose, dose rate, and type of radiation. A detailed discussion of deterministic effects and associated dose-response relationships is provided in the NUREG/CR-4214 report (NRC, 1989a).

Table 2.1, based on information in the NUREG/CR-4214 report (NRC, 1989a), lists the deterministic effects for which models were developed, as well as the organs for which absorbed radiation doses are required as inputs. Both human and animal data were used to develop the models. However, the models up until now are specific for exposure to low-LET radiation. The purpose of this addendum is to incorporate alpha radiation into the models where necessary.

2.2 Radiobiological Considerations

2.2.1 Data from Human Populations

Historically, very few accidental human exposures have involved inhalation of alpha-emitting radionuclides at a level at which deterministic effects would be expected. In reviews of data on USAEC contractor personnel who worked with various alpha-emitting radionuclides, no clinical evidence of

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[a]As recommended in ICRP Publication 60 (ICRP, 1991), the term "nonstochastic effects" has been replaced by "deterministic effects" in this report. Deterministic effects are defined as follows: "...those detrimental effects in a tissue or an organism, which occur only after high doses and which are observed to be dose dependent with respect to their severity as well as their frequency." Stochastic effects are those for which the severity is not dose dependent and the frequency increases with dose, without assumption of a threshold.

Table 2.1

Early and continuing effects included in models of health effects resulting from exposure to low-LET radiation (NRC, 1990a)

Effect	Model developed		Organ-dose
	Mortality	Morbidity	
Hematopoietic death	*	-	Bone marrow
Pulmonary death	*	-	Lung
Gastrointestinal death	*	-	Small intestine[a] - colon
Prodromal symptoms			
Vomiting	-	*	Abdomen[b]
Diarrhea	-	*	Abdomen[b]
Pneumonitis	-	*	Lung
Thyroid effects			
Thyroiditis	-	*	Thyroid
Hypothyroidism	-	*	Thyroid
Skin effects			
Erythema	-	*	Epidermis[c]
Transepidermal injury	-	*	Epidermis[c]
Cataracts	-	*	Lens of eye
Embryo/Fetus			
Microencephaly	-	*	Embryo/Fetus
Severe mental retardation	-	*	Embryo/Fetus
Death of embryo/fetus	*	-	Embryo/Fetus

[a] The dose to small intestine is used to estimate the risk from brief external exposure. The dose to the colon is used to estimate the risk from protracted internal exposure.

[b] Midline, midplane upper abdominal dose.

[c] Dose to the basal cells (about 0.1 mm depth) of an area of 50 to 100 cm^2.

deterministic effects of alpha irradiation of the lung was reported (Ross, 1968). For two cases that involved continuing deterministic effects in the lung after long-term exposure to alpha radiation from radon and radon progeny reported prior to the Chernobyl accident, it was not possible to estimate the radiation doses to the lung accurately (Doenecke and Bolt, 1931; Rajewsky, 1939). Also, Taube (1964) mentioned two fatal cases of plutonium poisoning but did not provide information on either the doses received or the nonfatal biological effects observed.

The plant personnel and auxiliary staff present at the site of the Chernobyl accident were exposed to a combination of extreme heat and radiations that may have included alpha radiation from internally deposited transuranics. However, the most significant radiation exposures were from external gamma radiation and from beta emitters deposited on the skin (UNSCEAR, 1988). Inhaled radionuclides such as radioiodine and cesium contributed only a minor part of the total radiation dose.

Plutonium contamination of vast areas in the Urals in Russia resulted from operations related to producing plutonium at the Mayak Complex located 15 km from the town of Kyshtym and 100 km from Chelyabinsk. A large population was exposed to plutonium and beta- and gamma-emitting radionuclides as a result of these operations. However, data on radiobiological effects resulting from these exposures are not currently available.

Most of our knowledge of the response of the human lung to alpha radiation has been obtained from miners who were exposed underground by inhalation to airborne uranium ore dusts, radon, and radon progeny. The primary biological effect observed in these miner populations was the occurrence of lung cancers many years after the beginning of these occupational exposures. This information is discussed in greater detail in Chapter 3.0, "Late Somatic Effects." The BEIR IV report (NAS/NRC, 1988) provides an extensive literature review of the health effects of radon and other alpha-emitting radionuclides. However, this committee did not report finding any data on the deterministic effects of alpha irradiation of the lung.

Studies of laboratory animals that inhaled large quantities of alpha-emitting radionuclides have provided most of what we know about the deterministic effects resulting from large radiation doses from alpha radiation. Therefore, these results form the foundation of the health effects models presented in this section of this report.

2.2.2 Studies in Laboratory Animals

Animal experiments were conducted for the NRC at the Pacific Northwest Laboratory (PNL) and at the Inhalation Toxicology Research Institute (ITRI) to generate data bases on the deterministic effects of combined, high-LET alpha and low-LET (beta or gamma) irradiation of the lung. These data were subsequently used to validate existing models or to develop improved models (NRC, 1987, 1988a,b, 1989b,c; Scott *et al.*, 1990).

In experiments at PNL, sublethal doses of total-body gamma radiation followed immediately by inhalation exposure to insoluble $^{239}PuO_2$ aerosols increased the lethality from deterministic effects in dogs and rats.

The cumulative alpha dose to 1 year from plutonium that led to 50% mortality when given in combination with gamma radiation was approximately one-half that which led to 50% mortality from plutonium alone. The data indicated that the enhancement effect of external gamma irradiation was greater in dogs than in rats (NRC, 1988a), owing to a higher sensitivity of dogs to death from injury to the hematopoietic system. However, respiratory functional morbidity, due to impaired lung function caused by the inhaled plutonium, was enhanced to a much lesser extent by total-body irradiation than was lethality.

With dogs, a total-body gamma dose of 2.35 Gy reduced the median alpha radiation dose required for 1-year lethality from all causes from 45 Gy to 20 Gy. This 25 Gy reduction in the dose to lung is not surprising because a brief exposure to 2.35 Gy to the total body is very near to the median lethal dose for hematopoietic death (LD_{50} = 2.43 Gy) (NRC, 1988a). The gamma radiation threshold for hematopoietic death is estimated to be about one-half of the median lethal dose (NRC, 1989a) or about 1.22 Gy to the total body. Based on the Weibull model developed for hematopoietic death in dogs (Scott *et al.*, 1988), 2.35 Gy of gamma radiation uniformly distributed over the body would be expected to lead to about 40% lethality from the hematopoietic mode.

Acute lethality data for rats that received a dose of external gamma radiation followed by inhalation exposure to $^{239}PuO_2$ provide additional information on the combined effects of alpha and gamma irradiation (NRC, 1988a). In this study, a median lethal dose of alpha radiation for 1-year lethality from lung injury in the rat was reduced from 58 Gy to 36 Gy when combined with total-body gamma doses of 8.5-9.15 Gy (mid-range - 8.83 Gy). Analyses of the survival-time distribution data suggested that sublethal, total-body gamma doses may have accelerated the development of lethal pulmonary lesions induced by chronic alpha irradiation. However, because of the 1-year duration of this study, the total impact of alpha plus gamma irradiation of the lung may not have been fully demonstrated.

Published estimates for the median lethal dose for pulmonary death following external photon irradiation of the thorax region in rats and mice were in the range of 11-15 Gy (mid-range - 13 Gy) when no palliative drugs were used in the treatment and when radiation pneumonitis was confirmed (Cardozo *et al.*, 1985; Down and Steel, 1983; Dunjic *et al.*, 1960; Kurohara and Casarett, 1972). These results, along with those discussed for alpha irradiation, indicate that considerable recovery occurs in rats during chronic alpha irradiation of the lung because the median lethal dose for pulmonary death from chronic alpha irradiation exceeds 40 Gy, while for brief exposure to external photons it is about 13 Gy. With no recovery, the median lethal dose for chronic alpha irradiation would have been less than that for a brief exposure to external photons. These results suggest that the RBE for deterministic effects of alpha irradiation of the lung should be estimated by comparing chronic alpha to chronic beta irradiation rather than to acute gamma irradiation (see section 2.2.3).

Muggenburg *et al.* (1988) demonstrated that alpha doses of 2.4 to 7.3 Gy to the lungs of dogs from $^{239}PuO_2$ caused clinical signs and pulmonary function indicators of restrictive lung disease at long times after inhalation of plutonium. Thus, unlike a brief exposure to external radiation, inhaled plutonium can induce radiation pneumonitis and pulmonary fibrosis, years after inhalation exposure.

With animal studies, the hematological effects of inhaled, relatively insoluble aerosols containing alpha-emitting radionuclides depend on species. Only minor effects have been seen in rats (NAS/NRC, 1988; NRC, 1988a; Scott *et al.*, 1990) and in monkeys (NAS/NRC, 1988). In dogs, however, significant lymphocytopenia has been observed after inhalation of $^{239}PuO_2$, $^{238}PuO_2$ or $^{239}Pu(NO_3)_4$ (Ragan, *et al.*, 1986). The degree of lymphocytopenia was influenced by the magnitude of the initial body burden and the chemical form of the plutonium. Animal studies have not demonstrated deterministic effects in the GI tract following inhalation exposure to alpha-emitting radionuclides.

2.2.3 RBE for Deterministic Effects of Alpha Radiation in Lung

In the chronic irradiation studies conducted at PNL in which rats inhaled ^{239}Pu or ^{147}Pm in insoluble aerosol forms, the effectiveness of chronic alpha radiation relative to chronic beta radiation for 1-year lethality was about 5 (NRC, 1988a, 1989c). Similar studies, in which rats inhaled ^{238}Pu or ^{147}Pm in insoluble aerosol forms, were performed at ITRI. For the latter studies, the biological effectiveness of alpha radiation relative to beta radiation was about 7, both for pulmonary death and for respiratory functional morbidity, based on 1.5-year mortality data and data for morbidity among 1.5-year survivors (NRC, 1988b).

An extensive review of animal data on deterministic effects was recently summarized in ICRP Publication 58. One goal of this review was to estimate the RBE for deterministic effects of chronic alpha relative to chronic beta irradiation of the lung (ICRP, 1990). Based on this review, the RBE for deterministic effects of chronic alpha irradiation of the lung appears to be in the range of 7-10.

ICRP Publication 58 also provided estimates of RBEs for the deterministic effects of chronic neutron irradiation. These values were based on the results of studies conducted with californium sources being investigated for use in intracavitary and interstitial brachytherapy. The responses of several types of normal tissues were investigated. In most studies, except for those in which cell cultures or skin were irradiated, only dose rates in the range of 0.05-0.5 Gy/h could be applied. The RBE values were obtained by comparing the effects of chronic neutron irradiation with the effects of low dose-rate gamma irradiations, e.g., from ^{226}Ra. Under these circumstances, the RBEs were observed to be in the range of 5-10 and were, therefore, consistent with values obtained for chronic alpha radiation relative to chronic beta irradiation of the lung. More importantly, the RBE was determined to have little dependence on dose, suggesting that for chronic irradiation, a fixed RBE could be used (NRC, 1988b; Scott *et al.*, 1990). In the revised model provided in Appendix 2A, a fixed value of the RBE is used for chronic alpha irradiation relative to chronic beta irradiation for predicting the combined deterministic effects of alpha, beta, and gamma irradiation. Gamma and beta irradiations are treated as being equally effective for the same dose-rate patterns. For chronic alpha irradiation of the lung, a central estimate of 7 is recommended for the RBE relative to chronic beta irradiation, with upper and lower estimates of 10 and 5, respectively.

2.3 NUREG/CR-4214 Models for Deterministic Effects

Before addressing the incorporation of alpha radiation into the models for deterministic effects, it is useful to review the basic structure of the models presented in the NUREG/CR-4214 report for low-LET irradiation (NRC, 1989a). Except for hypothyroidism, which was modeled with a linear-threshold function, the risk of each deterministic effect of interest was modeled by using the Weibull dose-response function evaluated on the basis of a normalized dose, X, where for low-LET radiation, X = 1 corresponds to an LD_{50} or ED_{50} absorbed dose, regardless of the dose-rate pattern (Yaniv and Scott, 1990; Scott *et al.*, 1988; NRC, 1987).

The normalized dose X depends on the dose-rate pattern, and its evaluation requires a dose-rate-dependent model for the LD_{50} or ED_{50} for the endpoint of interest (Scott *et al.*, 1988; Scott and Dillehay, 1990). A more general notation, D_{50}, is used to represent the LD_{50} and the ED_{50} in modeling dose-rate effects (NRC, 1989a). Increments in X are evaluated by taking increments, preferably small, in the absorbed dose to the tissue of interest and dividing each increment by the appropriate dose-rate-dependent D_{50}, evaluated at the average dose rate for which the increment in the absorbed dose is delivered. For example, if for a given relatively short time interval of interest the dose increment to the organ of interest (e.g., lung) was 2.4 Gy delivered at an average dose rate of 0.1 Gy/h, then the increment in X is simply calculated as the ratio 2.4 Gy/D_{50}, where the D_{50} in Gy is evaluated at the dose rate of 0.1 Gy/h. Increments in X obtained in consecutive time intervals are then added to obtain the total X. Normalized doses are larger for morbidity than for lethality for the same absorbed dose to a given organ or tissue. This result, which at first glance may seem backward, occurs because of the respective D_{50} values in the denominators of the normalized dose. A larger D_{50} value leads to a smaller normalized dose. For example, X doses for lethality from radiation pneumonitis are assumed to be about a factor of 2 times smaller than for morbidity due to impaired lung function (i.e., respiratory functional morbidity) based on animal data (NRC, 1989a).

To evaluate increments in X accurately over preselected, relatively short, time intervals, dose-rate-dependent models are needed; however, dose-rate-dependent models have only been developed for hematopoietic and pulmonary death. These models are called "dose-rate models." For other effects (vomiting, diarrhea, hypothyroidism, erythema of the skin, and transepithelial injury of the skin), only very crude models, in which dose rates were grouped into two broad ranges (greater than 0.06 Gy/h, and less than or equal to 0.06 Gy/h), have been developed. Doses delivered at dose rates greater than 0.06 Gy/h (0.1 rad/min) were defined as brief exposures and all brief exposures were treated as equally effective. Doses delivered at dose rates less than or equal to 0.06 Gy/h were defined as protracted exposures, and all protracted exposures were treated as equally effective; protracted exposures were treated as less effective than brief exposures. Thus, the ratio of the D_{50} for protracted exposure to that for brief exposure was fixed. However, the ratio depended on the endpoint considered. For other effects (thyroiditis, reproductive and *in utero* effects, and cataracts), model parameters were developed for either brief or protracted exposures, but not for both.

Although some dose-rate dependent models were included in the NUREG/CR-4214 report (1989a), the MACCS code (NRC, 1990b) currently has no capability to use these dose-rate models. The structures of the models for deterministic effects in the MACCS code are based on the acute health effects models described in the original NUREG/CR-4214 report (NRC, 1985).

For individuals over age 40, one-half as much absorbed dose to the lung was assumed to be required to produce early and continuing effects in the lung as was required for younger individuals. The assumed variation in sensitivity with age was based on human and animal data presented in the NUREG/CR-4214 publication (NRC, 1989a). The 40-year point was judgmental.

Risks are evaluated indirectly using hazard functions. Lethality or morbidity hazards (i.e., cumulative hazard functions), H, are calculated by using the following equation:

$$H = (\ln 2)X^V, \tag{1}$$

where the parameter V (shape parameter) determines the steepness of the dose-response curve. V depends on the endpoint modeled.

The risk of a specific radiation-induced effect is related to H by the equation:

$$\text{Risk} = 1 - \exp(-H). \tag{2}$$

Because risk is evaluated indirectly using a hazard function, this type of model has been called a "hazard-function model." Threshold effects were simulated by requiring H to be zero at or below the appropriate threshold dose X for the effect. For example, for pulmonary death, the threshold X dose was estimated to be 0.5.

Competing modes of death (hematopoietic death, gastrointestinal death, and pulmonary death) were modeled by adding the respective lethality hazards for each mode of death to obtain the overall lethality hazard, which was then entered into Equation 2 for H. Upper and lower bounds for model parameters were provided to facilitate the evaluation of uncertainties.

In the sections that follow, a means is provided for incorporating alpha radiation into Weibull hazard-function models for evaluating deterministic effects of radiation exposures.

2.4 Normalized-Dose Model for Lung with Alpha Radiation Included

The manner in which alpha radiation is incorporated into the normalized dose model for pulmonary death depends on the accident scenario considered. Details on how to include alpha radiation in the normalized model are provided in Appendix 2A. Results are summarized here.

The solution for the hazard function from Appendix 2A is:

$$H = \ln(2)\,(X_a + X_b + X_g + X^*)^V, \tag{3}$$

where X^* accounts for the contribution to the overall normalized dose from the high-dose rate, brief exposure to mainly external gamma radiation, X_g accounts for the contribution to protracted dose from gamma-emitting radionuclides, X_b accounts for the contribution to protracted dose from inhaled beta-emitting radionuclides, and X_a accounts for the contribution to protracted dose from inhaled alpha-emitting radionuclides. This solution is applicable to two types of exposure: (1) simultaneous exposure of the lung to alpha, beta, and gamma radiations from inhaled radionuclides; and (2) brief exposure to mainly external gamma radiation followed by protracted (simultaneous) exposure to alpha, beta, and gamma radiations from inhaled radionuclides. The nuclear power plant accident scenarios considered involved a brief exposure to external gamma radiation followed by protracted exposures to alpha, beta, and gamma radiations resulting from inhaled radionuclides.

For brief exposure to mainly external gamma radiation followed by protracted (simultaneous) exposure to alpha, beta, and gamma radiations, the total normalized dose is given by the sum $X_a + X_b + X_g + X^*$, where X^* accounts for the contribution to the total normalized dose from the high-dose-rate, brief exposure to mainly external gamma radiation. The dose X^* is needed only when the external gamma radiation dose rate exceeds 0.06 Gy/h (0.1 rad/min), when averaged over a reasonable time interval; otherwise, the external gamma radiation dose can be added to the internal gamma radiation dose with the total gamma radiation dose used in evaluating X_g. The dose rate of 0.06 Gy/h is the same as was used in the 1989 NUREG/CR-4214 publication to distinguish between brief, high-dose-rate and protracted, low-dose-rate exposures. For the sequential exposure scenario considered, X^* is given by (see Appendix 2A)

$$X^* = (D/\theta_\infty)^\eta, \tag{4}$$

where θ_∞ is the D_{50} for brief exposure to external radiation (θ_∞ = 10 Gy), and η is the shape parameter for external gamma irradiation only, divided by the shape parameter for the protracted (simultaneous) exposure that follows. Thus, $\eta = 12/7$ or 1.7. For brief exposure to external gamma radiation followed by protracted exposure to alpha and/or beta radiation, $\eta = 12/5$ or 2.4. It is demonstrated in the following section that this model adequately predicts pulmonary deaths in rats exposed briefly to gamma radiation followed by protracted exposure to alpha or beta radiation.

2.5 Model Validation

Experimental studies were carried out at ITRI to determine whether normalized alpha and beta radiation doses (X_a and X_b), based on a dose-rate-pattern-specific median lethal dose, were additive for simultaneous exposure of the lung of rats via inhalation of insoluble fused aluminosilicate particles containing different $^{238}Pu/^{147}Pm$ activity ratios. The predicted deaths, based on the model, and the

observed deaths are shown in Table 2.2; predicted deaths were calculated by assuming additivity of the normalized alpha and beta radiation doses (Scott *et al.*, 1990). The predicted and observed cases of respiratory functional morbidity are shown in Table 2.3; predicted cases were also calculated by assuming additivity of normalized doses (Scott *et al.*, 1990).

Data of Filipy *et al.* (NRC, 1988a) for pulmonary deaths in rats that received brief, total-body exposure to external ^{60}Co gamma radiation followed by protracted, alpha-particle irradiation of the lung (via inhalation of insoluble $^{239}PuO_2$), were also used for model validation. For rats exposed to Pu only, the median lethal dose for pulmonary death (based on 1-year follow-up) was 58 Gy to the lung. Brief exposure to 8.8 Gy (mid-range dose) of gamma radiation before protracted exposure to Pu alpha particles reduced the median lethal dose for pulmonary death from 58 to 36 Gy (additional alpha radiation dose) when hematopoietic deaths were eliminated from the data.

Table 2.2

Predicted and observed deaths from radiation pneumonitis (pulmonary deaths) within 18 months after inhalation exposure of rats to mixtures of ^{238}Pu and ^{147}Pm in fused aluminosilicate particles (Scott *et al.*, 1990)[a]

1.5-year dose to lung in Gy		Risk set size	Predicted deaths[b]	Observed deaths
Alpha	Beta			
8.7	30	9	0	0
56	45	22	17 ± 2	21
8.7	110	18	1 ± 1	1
45	150	32	25 ± 2.4	32

[a] D_{50} for exposure to ^{147}Pm only was 300 Gy (1.5-year dose); D_{50} for exposure to ^{238}Pu only was 45 Gy (1.5-year dose).

[b] Predicted deaths were calculated (Scott *et al.*, 1990) by using the ratio ILB/ILB_{50} as an estimate of normalized dose X for each radiation type; ILB is the initial lung burden (activity per gram lung), and ILB_{50} is the median lethal ILB. The same results are obtained when the 1.5-year absorbed dose and fixed D_{50} for the radionuclide and pattern of irradiation are used instead of the ILB and ILB_{50}. Risks were evaluated using the Weibull normalized dose model with a shape parameter of 5 for both alpha and beta irradiation.

Table 2.3

Predicted and observed cases of respiratory functional morbidity among 1.5-year survivors after inhalation exposure of rats to mixtures of ^{238}Pu and ^{147}Pm in fused aluminosilicate particles (Scott *et al.*, 1990)[a]

1.5-year dose to lung in Gy		Risk set size	Predicted cases[b]	Observed cases
Alpha	Beta			
8.4	104	19	18.5 ± 0.7	18
8.4	26	5	2.7 ± 1.1	4

[a] D_{50} for exposure to ^{147}Pm only was 75 Gy (1.5-year dose); D_{50} for exposure to ^{238}Pu only was 11 Gy (1.5-year dose).

[b] Predicted deaths were calculated (Scott *et al.*, 1990) by using the ratio ILB/ILB_{50} as an estimate of normalized dose X for each radiation type; ILB is the initial lung burden (activity per gram lung), and ILB_{50} is the median effective ILB. The same results are obtained when the 1.5-year absorbed dose and fixed D_{50} for the radionuclide and pattern of irradiation are used instead of the ILB and ILB_{50}. Risks were evaluated using the Weibull normalized dose model with a shape parameter of 5 for both alpha and beta irradiation.

Equations 3 and 4 can be used to predict the median lethal dose (additional alpha radiation dose) for the combined sequential exposure. The parameter θ_∞ in Equation 4 for pulmonary death in rats exposed to low-LET photons has been reported to be in the range 11 to 15 Gy to the lung as compared to 10 Gy for humans (NRC, 1989b). Using an estimate of 11 Gy for θ_∞, X^* is found to be $(8.83/11)^{2.4}$ or 0.59 using Equation 3. When an estimate of 15 Gy is used for θ_∞, X^* is found to be $(8.83/15)^{2.4}$ or 0.28. The median lethal dose for the combined gamma plus alpha radiation exposure will be achieved when the overall normalized dose ($X_a + X_b + X_g + X^*$) in Equation 3 equals one. Because there is no protracted beta or protracted gamma dose, both X_b and X_g equal zero, and the median lethal dose (additional plutonium alpha particle dose) can be predicted using the equation

$$X_a + X^* = 1, \tag{5}$$

by first finding X_a given by

$$X_a = 1 - X^*. \tag{6}$$

The normalized dose X_a corresponds to the additional alpha radiation dose needed to bring the risk of pulmonary death to 50% (NRC, 1989b) and is approximately equal to the ratio B/(58 Gy) where the 58 Gy is the median lethal dose obtained by Filipy *et al.* (NRC, 1988a) when 100% percent of the dose to the lung was from alpha radiation. The variable B is the absorbed alpha radiation dose (1-year dose) to

the lung needed to bring the overall risk for pulmonary death to 0.5 (or 50%). For X^* equal to 0.59, X_a equals 0.41 so that B equals (0.41)(58 Gy) or 24 Gy. Similarly, for X^* equal to 0.28, X_a equals 0.72 so that B equals (0.72)(58 Gy) or 42 Gy. Thus, with this modeling approach, one predicts B for the combined sequential exposure considered, to be in the range of 24 to 42 Gy (mid-range value 33 Gy) to the rat lung, while it was found by Filipy *et al.* (NRC, 1988a) to be 36 Gy.

The normalized dose approach was also used to predict the median lethal dose in rats that received brief total-body exposure to ^{60}Co gamma radiation (8.9 Gy to total body) followed by protracted beta-particle irradiation of the lung (*via* inhalation of ^{147}Pm in insoluble fused aluminosilicate particles). Predictions were based on a study conducted by Filipy *et al.* (NRC, 1989c). Using the normalized dose approach and a value of $\theta_\infty = 13$ Gy, the median lethal dose (additional beta dose to lung from ^{147}Pm) for the combined exposure was predicted to be 170 Gy as compared to the observed median lethal dose of 160 Gy (NRC, 1989c).

The normalized dose approach was used to predict 1-year lethality after sequential exposure of dogs to 2.35 Gy external ^{60}Co gamma irradiation of the total body followed by inhalation exposure to insoluble $^{239}PuO_2$, based on data from Filipy *et al.* (NRC, 1988a). In this study, exposure of the total body to gamma radiation led to a reduction in the median lethal dose (Pu alpha radiation) for 1-year lethality. A 25-Gy reduction in the median lethal dose (Pu alpha radiation dose) was observed, while an 18-Gy reduction was predicted using the normalized dose approach and modeling two competing risks (pulmonary and hematopoietic deaths) (NRC, 1989b). The reduction in the median lethal dose for 1-year lethality was mainly due to gamma-radiation-induced hematopoietic deaths.

Predictions based on use of normalized dose models are therefore in reasonable agreement with available animal data on deterministic radiobiological effects of simultaneous, internal alpha-plus-beta irradiation of lung, external gamma irradiation of the total body followed by internal beta irradiation of the lung, and external gamma irradiation of the total body followed by internal alpha irradiation of the lung.

Judgments about threshold doses can be made after calculating the gamma radiation equivalent prompt dose (EPD) by multiplying the total normalized dose X obtained by the high dose-rate median lethal dose for gamma irradiation given by θ_∞ to obtain the product $X\theta_\infty$. Central, lower, and upper estimates for θ_∞ based on the NUREG/CR-4214 report (NRC, 1989a) are 10, 8, and 12 Gy, respectively. The gamma-radiation EPD obtained in this way can be compared to the threshold EPD of 5 Gy. EPDs less than the threshold dose of 5 Gy would be associated with zero risk for pulmonary death. Upper and lower bounds for the 5 Gy estimate are 6 Gy and 4 Gy, respectively.

2.6 Summary

Based on results from studies in laboratory animals and very limited human data, the lung appears to be the most important organ at risk for deterministic effects from inhaled, relatively insoluble forms of alpha-emitting radionuclides that might be released in the event of an accident at a nuclear power plant. In the underlying NUREG/CR-4214 report (NRC, 1989a), risk estimates for the occurrence of deterministic effects in the lung were given for low-LET beta and gamma radiations. These risk estimates were based on a Weibull model that depends on normalized dose. The use of normalized dose facilitates accounting for dose-rate effects and makes it possible to include alpha radiation when required by the exposure scenarios being considered.

The recommended approach for computing the lethality or morbidity hazard and corresponding risk for a combined exposure that includes both low-LET beta and gamma radiations and high-LET alpha radiation is to: a) multiply the absorbed alpha radiation dose by the RBE for deterministic effects in the organ considered (use RBE=7 for the lung); b) add the product obtained to the low-LET dose rate; c) calculate the normalized dose in the same way as is done for low-LET radiation; and d) use the total normalized dose to compute the hazard and risk for the deterministic effect considered. To make these computations, a preferred value of 7 is recommended for the shape parameter in the Weibull model for early-occurring and continuing effects of combined (simultaneous) exposure of the lung to alpha, beta, and gamma radiations.

Model parameters for pulmonary deaths from deterministic effects in children or adults age 40 or less are given in Table 2.4 along with estimated values for the upper and lower bounds for these parameters. This table has been adapted from Table 2.14 in the NUREG/CR-4214 report (NRC, 1989a). For individuals over age 40, the listed D_{50} and threshold estimates should be reduced by a factor of 2.

Table 2.4

Model parameters for pulmonary deaths among young adults (age 40 or less) or children[a] (Adapted from Table 2.14, NUREG/CR-4214)

Exposure category	Adjusted dose rate[b] Gy/h	Calculated D_{50} (Gy)			Shape parameter			Threshold (Gy)		
		Central estimate	Lower estimate	Upper estimate	External radiation only[c]	Internal radiation only[d]	Both[e]	Central estimate	Lower estimate	Upper estimate
Brief[f]	≥ 100	10	8	12	12	NA[g]	NA[g]	5	4	6
Brief	10	15	10	20	12	NA	NA	7	5	9
Brief	1	40	20	60	12	NA	NA	20	10	30
Brief	0.5	70	40	100	12	NA	NA	40	20	60
Brief	0.1	310	160	460	12	5	7	160	60	230
Protracted[f]	0.05	610	310	910	12	5	7	310	160	460

[a] For individuals over age 40, D_{50}s and thresholds given should be divided by 2.
[b] Adjusted dose rate equals the low-LET dose rate plus 7 times the high-LET dose rate.
[c] Shape parameter has lower and upper bounds of 9 and 14, for external gamma irradiation (NUREG/CR-4214).
[d] Internal alpha, beta, and gamma irradiation.
[e] Both external irradiation (gamma) and internal irradiation (alpha, beta, and gamma).
[f] Brief implies adjusted dose rates equal to or greater than 0.06 Gy/h. Protracted implies adjusted dose rates below this range.
[g] NA implies not applicable to internal irradiation.

APPENDIX 2A
Incorporation of Alpha Radiation into Dose-Rate-Dependent Lung Models

To incorporate alpha radiation into the 1989 NUREG/CR-4214 model for pulmonary death, the normalized dose model was extended to include a normalized dose for high-LET radiation (NRC, 1989b). The normalized dose $X_{bg} = X_b + X_g$ represents the contribution of beta and gamma radiations to the total normalized dose X; where the subscript *bg* represents beta and gamma, *b* represents beta, and *g* represents gamma radiations. The remainder, X_a, comes from the high-LET radiation, with the subscript *a* indicating alpha radiation. This model only applies to simultaneous exposure. With this model, the dose-rate-dependent normalized doses X_a, X_b, and X_g, are additive (i.e., $X = X_a + X_b + X_g$) for a simultaneous exposure to alpha, beta, and gamma radiations. However, this should not be regarded as indicating that the different radiations act independently (Scott, 1989). For independent action, the radiation-specific hazard functions H_a, H_b, and H_g, for alpha, beta, and gamma radiations, respectively, would be additive, leading to a lethality hazard, H_{in}, given by

$$H_{in} = H_a + H_b + H_g = (\ln 2)X_a^{V_a} + (\ln 2)X_b^{V_b} + (\ln 2)X_g^{V_g}, \qquad (A.1)$$

for radiation-specific shape parameters V_a, V_b, and V_g, for alpha, beta, and gamma radiations, respectively. Note that with the independent action model, there is no interaction term (i.e., no cross-products of doses X_a, X_b, and X_g). Equation A.1 will usually be less than or equal to the lethality hazard, H, obtained by adding the normalized doses, which is given by

$$H = (\ln 2)(X_a + X_b + X_g)^V, \qquad (A.2)$$

where the shape parameter V for combined exposure to alpha, beta, and gamma radiations depends on the mixture (NRC, 1989b; Scott *et al.*, 1986) and is obtained as a solution to:

$$1/V = g_a/V_a + g_b/V_b + g_g/V_g. \qquad (A.3)$$

The variables g_a, g_b, and g_g represent the fraction of the total normalized dose due to alpha, beta, and gamma radiations, respectively. Expanding the righthand side of Equation A.2 leads to terms identical to those in Equation A.1, along with additional cross-products that represent expected interactions. The interaction term is quite complicated but, by definition, is equal to the difference, $H - H_{in}$, with H given by Equation A.2 and H_{in} given by Equation A.1.

Data discussed in Table 2.14 of the NUREG/CR-4214 publication (NRC, 1989a) indicated that for pulmonary death, $V_a = V_b = 5$, while $V_g = 12$. Unpublished results of more recent computer simulations indicate that a value as low as 3 may be needed for V when the dose-rate-dependent Weibull model from the 1989 NUREG/CR-4214 report is used instead of the 1985, fixed-parameter Weibull model (NRC, 1985), for cases where most of the dose to the lung is due to inhaled, beta-emitting radionuclides. For this reason, we recommend using 3 for a lower estimate of V.

A major unresolved question is why the dose-response curve is so steep (V=12) for external photon irradiation, as compared to internal alpha or beta irradiation (V=5). A possible contribution to the different curve shapes may be rather large errors in the alpha and beta radiation doses. This could flatten the dose-response curve (i.e., make it appear less steep). Age as a confounding variable may also distort the shape of the dose-response curve for chronic irradiation. However, more research is needed to resolve this question.

Calculated values of the shape parameter for pulmonary death are provided in Table 2A.1 for different contributions to the total normalized dose of gamma radiation and of alpha plus beta radiation. Alpha and beta radiation contributions were combined in generating Table 2A.1, because the shape parameters are the same for both radiations. Based on Equation A.3, the shape parameter V can change over time if the contributions of alpha, beta, and gamma radiations change with time. However, the accommodation of a time-dependent shape parameter would require modification of Equation A.2 and would be too cumbersome, and perhaps too costly, to incorporate into software such as MACCS (Jow and Sprung, 1990; NRC, 1990b), which was used to implement the 1985 models (NRC, 1985). For this reason, the fixed value, V = 7, is recommended. This value occurs when one-half of the normalized dose is due to gamma radiation and one-half is due to alpha and beta radiation, and should be used for central risk estimations for simultaneous exposure to alpha, beta, and gamma radiations. In the 1989 NUREG/CR-4214 publication (NRC, 1989a), a value of 7 was also used, based on one-half of the normalized dose arising from external gamma radiation and one-half from internal beta radiation. Upper and lower estimates for the shape parameter, 12 and 5, respectively, were provided for mixtures of different radiations in the 1989 NUREG/CR-4214 publication. For reasons previously pointed out, changing the lower estimate from 5 to 3 is also recommended.

The sum, $X_a + X_b + X_g$, in Equation A.2, which represents the total normalized dose X, is the solution to the equation

$$X = \int dX = \int (DR/\theta(DR))dt, \tag{A.4}$$

where the adjusted dose rate, DR, in Gy, is given by

$$DR = (RBE_a)DR_a + DR_b + DR_g, \tag{A.5}$$

for radiation-specific dose rates DR_a, DR_b, and DR_g; for alpha, beta, and gamma radiations; and for an alpha RBE (i.e., RBE_a), which has been estimated to be approximately 7 for the deterministic effects of irradiation of the lung. The function $\theta(DR)$ represents the D_{50} evaluated at adjusted dose rate DR. The integral in Equation A.4 is evaluated over the exposure period for which significant radiation dose is accumulated.

Table 2A.1

Shape parameter for simultaneous exposure of the lung to alpha, beta, and gamma radiations as a function of the fraction of the total normalized dose due to gamma and alpha plus beta radiation

Fraction of total normalized dose		
Gamma radiation	Alpha and beta radiations	Shape parameter V[a]
0.0	1.0	5.0[b]
0.1	0.9	5.3
0.2	0.8	5.7
0.3	0.7	6.1
0.4	0.6	6.5
0.5	0.5	7.1
0.6	0.4	7.7
0.7	0.3	8.5
0.8	0.2	9.4
0.9	0.1	10.5
1.0	0.0	12.0[c]

[a] Lower bound of 3 and upper bound of 12, except when all of the dose is due to single type of radiation.

[b] Appropriate for 100% of dose due to beta or alpha radiation (NRC, 1989a,b).

[c] Appropriate for 100% of dose due to external gamma radiation (NRC, 1989a,b).

Substituting the expression for DR from Equation A.5 into Equation A.4 leads to the sum of three integrals

$$X = RBE_a \int (DR_a/\theta(DR))dt + \int (DR_b/\theta(DR))dt + \int (DR_g/\theta(DR))dt, \quad (A.6)$$

$$X_a = RBE_a \int (DR_a/\theta(DR))dt, \quad (A.7)$$

$$X_b = \int (DR_b/\theta(DR))dt, \quad (A.8)$$

$$X_g = \int (DR_g/\theta(DR))dt. \quad (A.9)$$

Approximate estimates of X_a and X_b can be obtained by dividing the absorbed alpha and beta doses, evaluated to a fixed time (e.g., 1 year), by the corresponding alpha and beta radiation-pattern-specific D_{50}s, evaluated to the same time (Scott *et al.*, 1990).

The dose-rate model used to evaluate θ(DR) is given by

$$\theta(\mathrm{DR}) = \theta_1/\mathrm{DR} + \theta_\infty, \tag{A.10}$$

where θ and θ_∞ are positive parameters. For very high adjusted dose rates (e.g. 10 Gy/h) that overwhelm repair and recovery mechanisms, θ(DR) approaches the asymptotic value θ_∞ in Gy, which represents the D_{50} for prompt exposure.

The EPD in Gy is therefore given by

$$\mathrm{EPD} = X\theta_\infty, \tag{A.11}$$

where θ_∞ = 10 Gy. For individuals over 40, X is evaluated to be twice as large as for individuals of 40 years old or younger as recommended in the NUREG/CR-4214 publication (NRC, 1989a). The threshold EPD was estimated to be 5 Gy in the 1989 NUREG/CR-4214 publication, for individuals of age 40 or younger. EPDs are used in MACCS to implement crude hazard-function models.

For exposures at very high dose rates, Equation A.6 can be shown to reduce to an expression that depends on the fraction f_a of the total absorbed dose D due to alpha radiation and the fraction f_{bg} due to beta and gamma radiations because at high dose rates, D_{50}(DR) approaches a fixed value independent of dose rate. This leads to the useful relationship for high dose-rate exposures given by

$$X = (f_a/\theta_a + f_{bg}/\theta_{bg})D, \tag{A.12}$$

where $\theta_a = \theta_{bg}/\mathrm{RBE}_a$ represents the high-LET D_{50} in Gy for prompt exposure to alpha radiation, and $\theta_{bg} = \theta_\infty$ represents the D_{50} in Gy for prompt exposure to low-LET beta and gamma radiations.

A useful expression can be obtained from Equation A.12 related to the D_{50} for the combined exposure when it is expressed as the total absorbed alpha and low-LET dose in Gy. The expression is obtained by setting X = 1 in Equation A.12, replacing D with D_{50}, and rearranging to obtain the reciprocal relationship (Scott *et al.*, 1986; Scott, 1988)

$$1/D_{50} = f_a/\theta_a + f_{bg}/\theta_{bg}, \tag{A.13}$$

where the D_{50} is in Gy of alpha plus low-LET radiations. It follows from Equation A.13 that the RBE for the combined alpha plus low-LET, high dose-rate exposure is given by the linear relationship

$$\mathrm{RBE}_{mix} \text{ for combined alpha plus low-LET exposure} = 1 + (\mathrm{RBE}_a\text{-}1)f_a, \tag{A.14}$$

where $\mathrm{RBE}_a = \theta_{bg}/\theta_a$ = the RBE for alpha radiation. Note that the RBE for the mixture (RBE_{mix}) is predicted to be linearly related to the fraction of the total absorbed dose due to alpha radiation. The prediction is valid when the shape parameter in the Weibull model is the same for alpha and low-LET radiation. A straight-line plot of RBE_{mix} vs. f_a should have a slope equal to one less than the RBE_a;

should intersect the ordinate at a value of $f_{bg} = 1$ ($f_a = 0$); and should take on a value equal to the RBE_a, when $f_a = 1$.

While Equation A.14 is derived for combined alpha and low-LET beta and gamma irradiation of the lung, similar relationships would apply to other organs (e.g., bone marrow) and other mixtures of high- and low-LET radiations (e.g., mixed neutron-gamma fields). This is shown graphically in Figure 2A.1. Results are presented for deterministic effects in lung and bone marrow. Results for bone marrow are discussed later.

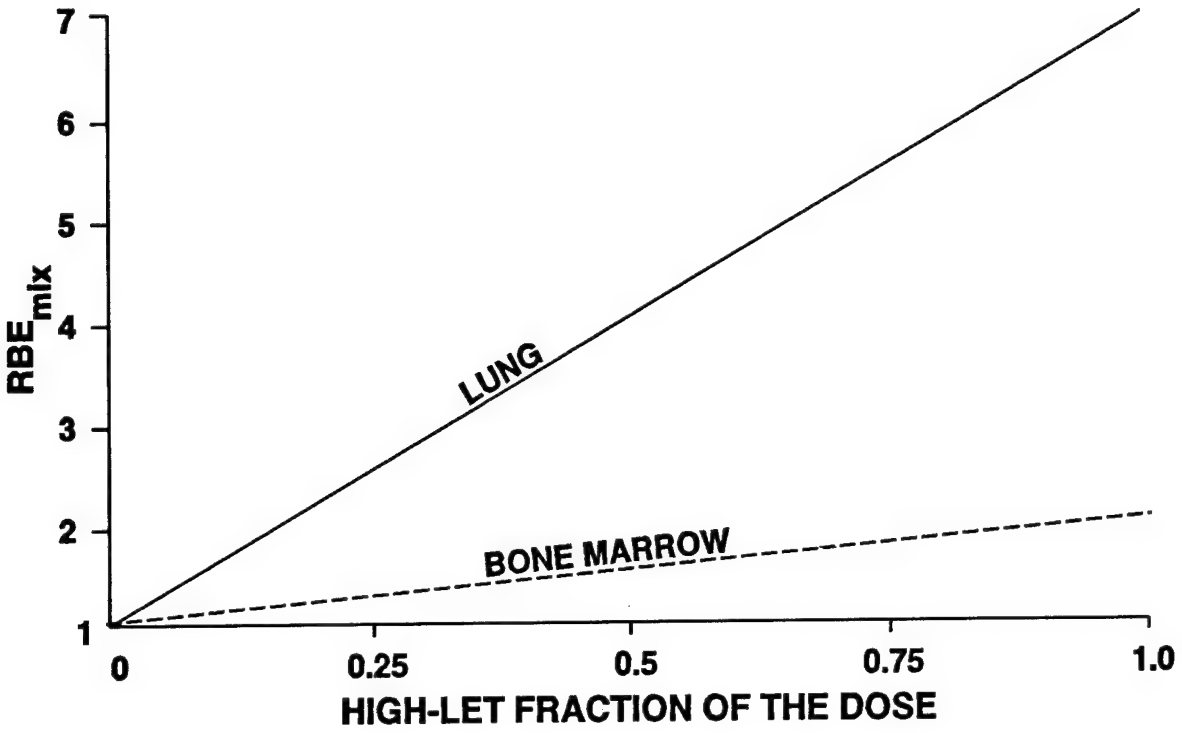

Figure 2A.1 Predicted linear relationships between RBE_{mix} for deterministic effects and the fraction of the total dose due to high-LET alpha radiation, for combined, high dose-rate exposure of the lung or bone marrow to alpha and low-LET beta and gamma radiations. It was assumed that beta and gamma radiations were equally effective for the same pattern of irradiation. The slope of the organ-specific curve is equal to one less than the RBE for the alpha radiation. For deterministic effects in lung, a value of 7 was used for RBE_a; for bone marrow, a value of 2 was used.

As an example of the application of the dose-rate-dependent model, the risk of pulmonary death has been calculated for a hypothetical scenario for which one-quarter of the normalized dose to the lung is due to alpha radiation, one-quarter due to beta radiation, and one-half due to gamma radiation. The resulting risks, presented in Table 2A.2, were calculated assuming independent action ($Risk_{in}$) and additivity of normalized alpha, beta, and gamma doses (Risk). Note that pronounced synergistic effects are predicted based on assuming additivity of normalized doses. If there are no interaction effects, the two models yield the same risk.

Equations A.2 through A.14 apply to simultaneous exposure to alpha, beta, and gamma radiations. However, for some nuclear reactor accident scenarios, brief exposure at a relatively high dose rate to mainly external gamma radiation (from the radioactive cloud and contaminated soil) will be followed by a period of protracted internal exposure to alpha and/or beta and gamma radiations from inhaled radionuclides. For this exposure scenario, the contribution X^* to the overall normalized dose arising from the high dose rate exposure to mainly external gamma radiation should be evaluated using the equation (NRC, 1989b)

$$X^* = (D_g/\theta_\infty)^\eta, \tag{A.15}$$

where D_g is the brief-exposure, gamma radiation dose, and η is the ratio of the shape parameter for external gamma irradiation to that for the combined exposure that follows. For brief exposure to mainly gamma radiation followed by protracted exposure to alpha and/or beta radiations, $\eta = 12/5$ or 2.4 (NRC, 1989b). For scenarios involving brief exposure to mainly gamma radiation followed by protracted exposure to alpha and/or beta and gamma radiations, it is recommended that η be set equal to 12/7 or 1.7. The value of 7 corresponds to the preferred shape parameter for simultaneous exposure to alpha, beta, and gamma radiations and was derived by assuming one-half of the protracted dose to the lung is due to alpha and beta radiation and the other one-half is due to protracted gamma radiation.
For such sequential exposure scenarios, Equation A.2 should be replaced by

$$H = \ln(2)(X_a + X_b + X_g + X^*)^V, \tag{A.16}$$

where X^* accounts for the contribution to the overall, normalized dose from the high-dose-rate, brief exposure to mainly external gamma radiation, X_g accounts for the contribution to protracted dose from inhaled gamma-emitting radionuclides, X_b accounts for the contribution to protracted dose from inhaled beta-emitting radionuclides, and X_a accounts for the contribution to protracted dose from inhaled alpha-emitting radionuclides.

Although Equation A.16 was derived for brief exposure at high dose rate to mainly external gamma radiation followed by protracted internal exposure to alpha, beta, and gamma radiations, it can also be used for simultaneous protracted exposure to alpha, beta, and gamma radiations (with external gamma radiation included). In this case, one simply sets $X^* = 0$ and combines the external and internal gamma radiation doses when determining X_g. Thus, only Equation A.16 needs to be incorporated into the computer code used for nuclear accident risk assessment.

Table 2A.2

A comparison of risks for pulmonary death calculated assuming either independent action ($risk_{in}$) or additivity of normalized alpha, beta, and gamma doses (risk) for $f_a = f_b = 0.25$, and $f_g = 0.5$[a]

X	Gamma EPD (Gy)	H_{in}	H	$Risk_{in}$	Risk
0.5	5	0.0000	0.0054	0.00	0.00[b]
0.6	6	0.0001	0.0194	0.00	0.02
0.7	7	0.0002	0.0571	0.00	0.06
0.8	8	0.0005	0.145	0.00	0.14
0.9	9	0.0008	0.332	0.00	0.28
1.0	10	0.0015	0.693	0.00	0.50
1.1	11	0.0027	1.35	0.00	0.74
1.2	12	0.0049	2.48	0.00	0.92
1.3	13	0.0090	4.35	0.01	0.99
1.4	14	0.0169	7.31	0.02	1.00

[a] This example corresponds to the case of simultaneous exposure where one-quarter of the dose X is due to alpha radiation, one-quarter due to beta radiation, and one-half due to gamma radiation. In this case:

$$H_{in} = 2(1n\ 2)\ (X/4)^5 + (1n\ 2)\ (X/2)^{12},$$

$$H = (1n\ 2)X^7,$$

$$Risk_{in} = 1 - \exp(-H_{in}),$$

and

$$Risk = 1 - \exp(-H).$$

[b] Risks at or below the threshold EPD of 5.0 Gy were set to zero. For individuals over age 40, the normalized doses, X, will be twice as large as for individuals 40 years old or younger. The higher normalized dose arises because the D_{50} for those over age 40 is one-half that for those age 40 or less.

For implementation of the code, it is recommended that X^* be set equal to zero when the external gamma radiation average dose rate for a given code-specific time interval is less than 0.06 Gy/h. The dose rate of 0.06 Gy/h was used in the 1989 NUREG/CR-4214 publication (NRC, 1989a) to distinguish between high and low dose rates of low-LET radiation. If X^* is set equal to zero, then the external gamma dose should be included when evaluating X_g.

The approach outlined above for the inclusion of alpha radiation could also be applied to hematopoietic death, provided one has an estimate of RBE_a for deterministic effects of irradiation of bone marrow. Estimates of the RBE for early effects in the hematopoietic system of mice for high-LET neutrons and heavy ions (carbon, neon, and argon), relative to low-LET photons, were summarized in ICRP Publication 58 (ICRP, 1990). The estimates ranged from about 1 to 3. Based on these results, it is suggested that a value of 2 be used for RBE_a to generate central risk estimates for hematopoietic death; a value of 1 when generating lower bound risk estimates; a value of 3 when generating upper bound risk estimates. A value of 2 was used to generate the curve for RBE_{mix} presented in Figure 2A.1.

If one assumes that the shape parameters for external gamma irradiation and for internal alpha and beta irradiation are the same for hematopoietic death, the alpha radiation dose rate to bone marrow can be multiplied by RBE_a and the results obtained added to the beta and gamma radiation dose rate to obtain the adjusted dose rate DR (e.g., in Gy/h) for the combined exposure that occurs. The total normalized dose X for hematopoietic death can then be evaluated using Equations A.4 and A.10, with θ_∞ equal to 3.0 Gy (lower and upper bounds of 2.5 and 3.5 Gy, respectively) and θ_1 equal to 0.072 Gy^2/h (with lower and upper bounds of 0.06 and 0.084 Gy^2/h, respectively) (NRC, 1989a). The lethality hazard for hematopoietic death can then be evaluated using

$$H = 1n(2)X^V. \qquad (A.17)$$

Modified lower and upper bounds on the shape parameter V can be used to account for additional uncertainty about what shape parameter to use for the combined low- and high-LET exposure of bone marrow. The previous lower and upper bound estimate of 4 and 8 for the shape parameter for low-LET radiation-induced hematopoietic death should be changed to 3 and 9, respectively, when high-LET alpha radiation is included.

The lethality hazard for hematopoietic death should be added to the lethality hazards for pulmonary and gastrointestinal deaths to obtain the total lethality hazard for death from early effects. Because of the short range of alpha particles in the gastrointestinal tract, alpha radiation dose to the gastrointestinal tract can be neglected when evaluating the early mortality risk.

3.0 LATE SOMATIC EFFECTS

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3.1 Introduction

Persons whose exposure to accidentally released radionuclides does not lead to mortality from the early-occurring effects discussed in Chapter 2 will be at risk from late-occurring somatic effects of low-LET or alpha irradiation, or both. In this chapter, we will discuss results of epidemiological studies and studies in laboratory animals conducted to examine the late-occurring somatic effects and to generate risk coefficients associated with chronic irradiation from internally deposited alpha-emitting radionuclides. With this information in hand, these results will be used along with models presented in Addendum 1 to obtain a model that will allow estimation of cancer risks associated with combined exposure to alpha and low-LET beta and gamma radiations in the event of an accident at a nuclear power plant.

As previously stated, the major mode of exposure to alpha-emitting radionuclides following an accident at a nuclear power plant is likely to be by inhalation of airborne radioactive particles. In considering the risks of late-occurring somatic effects, we have relied on earlier and recent publications (Bair *et al.*, 1974; BIR, 1989; Dolphin *et al.*, 1974; Gössner *et al.*, 1986; ICRP 1980, 1991; NAS/NRC 1976, 1988, 1990; NCRP 1975, 1990; and Nenot and Stather, 1979) as well as other publications cited throughout the text.

For actinides that might be released, especially isotopes of plutonium, americium, and curium, the organs most likely to receive potentially harmful radiation doses and to exhibit long-term effects are the lung, liver, and skeleton (ICRP, 1980). The following information is directed primarily to late-occurring somatic effects in these organs. Health effects information is summarized briefly for each of these organs followed by a section discussing the choice of risk coefficient for estimating late somatic effects in that organ.

3.2 Radiobiological Considerations and Risk Estimates

The health risks of late-occurring somatic effects of an inhalation exposure to airborne radionuclides can be modified by a number of parameters that influence the relationships between a) the inhalation exposure and the resulting dose to critical tissues, and b) the dose to critical tissues and the late-occurring somatic effects. Potential health risk modifiers for inhaled radionuclides include total dose, dose rate, LET, non-uniformity of irradiation, age, sex, health status, and species (ICRP, 1980; Thompson and Mahaffey, 1986; NAS/NRC, 1988; Stannard, 1988). Most of our knowledge on the temporal and spatial patterns of dose and response for inhaled radioactive materials has been derived from studies in laboratory animals. These studies have made it possible to investigate highly toxic materials in both serial-sacrifice and life-span studies that could not be conducted in human populations. Thus, these studies provide an

important knowledge base to supplement the information obtained from human populations exposed medically or occupationally to various isotopes and decay products of the naturally occurring radionuclides ^{235}U, ^{238}U, and ^{232}Th such as dial painters (exposed to ^{226}Ra) or uranium miners (exposed to radon and radon progeny). In the material that follows, we indicate sources of useful data from epidemiological studies of human populations and from studies in laboratory animals.

3.2.1 Lung

3.2.1.1 Data from Human Populations

The effects of occupational exposure to plutonium have been studied in workers in the Manhattan project (Voelz and Lawrence 1991), at the Los Alamos National Laboratory (Voelz *et al.* 1983), at Rocky Flats Nuclear Weapons Plant (Wilkinson *et al.* 1987), and at the Hanford Site (Gilbert *et al.* 1989a) with the results of most of these studies summarized by Tietjen (1987). No evidence of excess lung cancer in exposed members of these cohorts has emerged, but these negative findings could easily have been due to the limited power of these studies. In general, data from these studies are inadequate for risk estimation, because sample sizes and doses were too small, and because of difficulties in estimating doses to specific organs.

The only epidemiological data presently available that are adequate for estimating lung cancer risks produced by alpha-emitting radionuclides are the studies of underground miners exposed by inhalation to radon, radon progeny, and to other airborne contaminants. These data have been analyzed extensively and used as the basis for estimating lung cancer risks resulting from radon exposure. Models for estimating the risks of lung cancer from exposure to radon and radon progeny have been developed by the NCRP (1984), ICRP (1987), BEIR IV Committee (NAS/NRC, 1988), and others. Lifetime risk estimates based on several of these models are provided in Table 3.1 as a function of the cumulative exposure expressed per 10^6 person-WLM*. However, preferred risk estimates developed in this report for lung cancer induction by transuranic alpha emitting radionuclides are not based on miner data.

The NCRP (1984) model, which is based on an absolute risk that declines with time after exposure, yields a risk coefficient of 130 lung cancer deaths per 10^6 person-WLM. The ICRP (1987) model is based on an excess relative risk coefficient that is constant with respect to time after exposure and age at risk, but which is three times larger for those exposed under age 20 than for those exposed at age 20 and over. The ICRP Committee evaluated published analyses of several miner cohorts and determined an average excess relative risk coefficient of 1% per WLM. For use in the ICRP model, this coefficient was reduced by a factor of 0.7 to account for the combined effects of differing conditions in mine and indoor atmospheres and the result of 0.7% per WLM was used as the coefficient for those exposed at ages 20 and over. A coefficient of 2.1% was used for those exposed under age 20. The ICRP applied these

*Working level (WL) is defined as any combination of short-lived radon daughters in 1 liter of air that results in the ultimate release of 1.3×10^5 MeV of potential alpha energy. An exposure resulting from inhalation of air with a concentration of 1 WL of radon daughter for 170 h represents 1 working-level month (WLM).

Table 3.1

Lifetime risk estimates (based on several models) for fatal lung cancer resulting from inhalation of radon and radon progeny

Reference	Model	Excess lung cancer deaths per 10^6 person-WLM	Excess lung cancer deaths per 10^4 person-Gy[a]
1. NCRP (1984)	Declining absolute risk	130	260
2. ICRP (1987)	Constant relative risk 2.1% per WLM (age <20) 0.7% per WLM (age ≥20)	460	920
3. BEIR IV (NAS/NRC, 1988)	Declining relative risk	350	700
4. BEIR IV with treatments of age at exposure used in Addendum 1 (NRC, 1991)	Constant relative risk		
	a) 1.4% per WLM	520	1040
	b) 2.8% per WLM (age <20) 1.4% per WLM (age ≥20)	730	1460
	c) 4.2% per WLM (age <20) 1.4% per WLM (age ≥20)	930	1860

[a] Based on assumption that these cancers all originated in the bronchial epithelium and that the dose conversion factor for this region is about 5 mGy/WLM (BEIR IV report; NAS/NRC, 1988).

coefficients to baseline risks that were considered typical of a world population. However, if these coefficients are applied to U.S. lung cancer rates, a lifetime risk of 460 per 10^6 is obtained. The BEIR IV model, the most recent of these three models, was based on analyses of data from four miner cohorts (NAS/NRC, 1988). The model given in Table 3.1 represents the final model selected by the BEIR IV Committee, which included a decline in the excess relative risk with both time after exposure and age at risk.

The other three entries in Table 3.1 are based on use of different risk coefficients in the NUREG/CR-4214 modeling approach (NRC, 1989a). The first of these is based on the relative risk coefficient obtained by the BEIR IV Committee when a constant relative risk (without the declines with time and age noted above) was assumed, and yielded an excess relative risk coefficient of 1.4% per WLM

(NAS/NRC, 1988). Entry 4(a) in Table 3.1 gives the result of using this coefficient in the NUREG/CR-4214 models (NRC, 1989a).

The central and upper bound estimates for lung cancer risks, based on the model described in Addendum 1 to NUREG/CR-4214 (NRC, 1991), were derived assuming higher risks for those exposed under age 20 than for those exposed later in life. Specifically, the central and upper bound estimates are based on the assumptions that the excess relative risk coefficients for those exposed under age 20 are double and triple, respectively, the risks for those exposed at age 20 and older. Lifetime risk estimates including these age effects and using a coefficient of 1.4% per WLM for those exposed at age 20 and over are also shown as entries 4(b) and (c).

As discussed in Section 3.4.4 of Addendum 1 for low-LET radiation (NRC, 1991), the effects of time after exposure and age at exposure on lung cancer risks are uncertain, and it is primarily these uncertainties that lead to the variation in risk estimates presented in Table 3.1. The time after exposure and age at exposure effects for exposure to alpha-emitting radionuclides other than radon (such as plutonium, americium and curium) are even more uncertain. If one chooses to estimate lung cancer risk from transuranic alpha-emitting radionuclides based on miner data, a model in which time after exposure and age at exposure are handled in the same manner as in the lung cancer risk model for low-LET exposure seems reasonable (see Table 3.1, model 4(b)). This model leads to larger lifetime risk estimates than would most of the alternative treatments of time since exposure and age at exposure presented in Table 3.1.

All of these estimates are based on a unit of exposure, WLM, and not on absorbed dose to the respiratory tract. The dose received by critical cells in the bronchial epithelium is the key piece of information required to convert from exposure to dose because most of the observed lung cancers originate in the bronchial region. Estimates of this conversion factor range from about 4 to 13 mGy per WLM (ICRP, 1991). If one selects a factor of 5 mGy per WLM as was done in the BEIR IV report, the central estimate given in section 4(b) of Table 3.1 changes from 730 lung cancers per 10^6 person WLM to 1460 lung cancers per 10^4 person-Gy for persons exposed to radon and radon progeny. Using a factor of 10 mGy/WLM, a figure also within this range of values, would give 730 lung cancers per 10^4 Gy.

For the purposes of this report, these results for exposure to radon and radon progeny are primarily of interest to the extent that they provide information on the response of the pulmonary region to chronic alpha irradiation because that is the region of the respiratory tract of primary concern for inhaled transuranic radionuclides because of the prolonged retention in this region. Various approaches are used to define the relative radiosensitivity of the bronchial and pulmonary regions (Masse and Cross, 1989). In the meantime, one approach is to make the simple assumption that the risk coefficient for actinides in the pulmonary region equals the risk coefficient for radon and radon progeny in the bronchial region. This risk coefficient was computed above to be about 1500 lung cancers per 10^4 person-Gy based on the NUREG/CR-4214 modeling approach (NRC, 1989a). Because there are some indications that the pulmonary region may be less sensitive to radiation than the bronchial region (Masse and Cross, 1989), this estimate may overstate the risk of cancer in the pulmonary region.

3.2.1.2 Studies in Laboratory Animals

The absence of adequate human data on risks from inhaled, alpha-emitting radionuclides other than radon and its progeny has made it necessary to use other approaches to examine dose-response relationships for these types of exposure. A broad range of studies has been, and is being, conducted in various species and strains of laboratory animals to examine the effects of various dose- and effect-modifying factors. Major findings of these studies have been summarized in a number of reports including ICRP Publication 31 (ICRP, 1980), the BEIR IV report (NAS/NRC 1988), Stannard (1988), and Thompson (1989). Much of the information in this section has been drawn from these sources and their reference lists.

As noted in Chapter 1, inhaled, alpha-emitting, transuranic radionuclides that are deposited in the non-ciliated alveolar or pulmonary region of the lung are retained for prolonged periods of time. The range of alpha emissions in the pulmonary region, comprising cells and air space, is very short ($\sim$ 100-200 μm); the radiation doses received by various cells and tissues in the pulmonary region are therefore inherently less uniform than those received from deposited, energetic beta-emitting radionuclides or from external X or gamma radiation (Diel, 1978).

Studies in laboratory animals have also shown that alpha-emitting actinides are not deposited uniformly throughout the lung. Inhalation of a more soluble form leads to a more uniform distribution of radionuclide throughout the lung than that which occurs after inhalation of a more insoluble form. For instance, inhaled Am and Cm oxides, because of their higher solubility, are distributed more uniformly than $^{239}PuO_2$ (NAS/NRC, 1988). Subsequent dose-response studies in laboratory animals have also demonstrated a greater effectiveness of alpha irradiation of the lung when the dose is more uniformly distributed over the organ than for a more nonuniform irradiation (NCRP, 1975; Nenot and Stather, 1979; Bair *et al.*, 1974; Dolphin *et al.*, 1974; Medical Research Council, 1975; NAS/NRC, 1976; Gilbert *et al.*, 1989b). Much remains to be learned about the patterns of radionuclide re-distribution as a function of time after the inhalation exposure and how this re-distribution might impact the effectiveness of the emitted radiations.

Several different species of laboratory animals, such as the mouse, rat, Syrian hamster, dog, and non-human primate, have been used to study the induction of lung tumors by alpha-emitting radionuclides. Rats and dogs have been used in most of these studies. Three main types of lung tumors observed have been squamous cell carcinomas, adenocarcinomas, and sarcomas. In studies with dogs, adenocarcinomas have been the main type of lung tumors seen. It is important to note that the tumors seen in laboratory animals after exposure to alpha-emitting, transuranic radionuclides originate primarily in the alveolar and small bronchiolar regions of the lung. In contrast, most lung tumors in people, regardless of cause (such as inhalation of radon progeny or cigarette smoke), occur in the larger airways. Investigations continue on the reasons for such regional differences in the respiratory tract including species- or toxicant-related differences in dosimetry and/or carcinogenic responses.

A number of major life-span studies of dogs and rodents that inhaled ^{238}Pu or ^{239}Pu are being completed. Brief comments on the observed results are given below.

Results from ongoing studies in dogs at PNL suggest a quadratic dose response for the age-specific risk for alpha-radiation-induced lung cancer (Dagle *et al.*, 1986, 1989). In these studies, lung cancer risks are being evaluated in Beagle dogs given single inhalation exposures to aerosols of $^{239}PuO_2$, $^{238}PuO_2$, or $^{239}Pu(NO_3)_4$. Risks (per unit of dose) were found to differ for the three aerosols, and these differences were probably related to differences in the temporal and spatial distribution of the radiation dose.

In a large life-span study, Sanders *et al.* (1991) have been studying the dose-response relationship for tumors induced in female Wistar rats that inhaled $^{239}PuO_2$. Important features of this study include the large number of exposed and control rats used (3192) and the low total alpha doses to lung being studied (down to 0.07 Gy). The importance of using relatively low doses in studies of this kind to avoid artificially lower risk values obtained at higher doses, presumably due to wasted radiation at the higher doses, was emphasized by Cuddihy (1982). Although the histopathology for animals that received the lower doses is still incomplete, the dose-response curve for malignant lung tumors is clearly non-linear and may be described by a quadratic function. The data appear to be consistent with a possible "threshold" in the dose range of 1 to 2 Gy (Sanders and Lauhala, 1992). Final analysis and interpretation of these results must await completion of the remaining histopathology.

Life-span studies involving large numbers of F344 rats that inhaled $^{239}PuO_2$ aerosols are also being conducted at ITRI. Lundgren *et al.* compared the pulmonary carcinogenic response in rats that inhaled $^{239}PuO_2$ in one or seven repeated exposures. Using a linear logistic model, the prevalence of lung tumors per Gy of alpha dose to the lung appeared to be lower in the repeatedly exposed animals. For singly exposed groups of rats with lifetime pulmonary doses of <5 Gy, the risk coefficients for lung cancer ranged from 1500 to 2000 cancers/10^4 rat-Gy. A similar life-span study was conducted in F344 rats that received single or repeated inhalation exposures to $^{144}CeO_2$ which resulted in pulmonary irradiation by energetic beta radiation (Lundgren *et al.* 1992a,b). Because the experimental approaches were similar in both the $^{239}PuO_2$ and $^{144}CeO_2$ studies and involved large numbers of animals, these studies provided a direct experimental comparison of the carcinogenic effectiveness of alpha vs. beta irradiation of the pulmonary region. An analysis of the risk coefficients in rats that inhaled $^{239}PuO_2$ or $^{144}CeO_2$ in these two major studies resulted in an estimated RBE in the range of 23 to 26 with a midrange value of approximately 24 (Lundgren *et al.*, 1992b; Hahn *et al.*, 1992). The RBE estimates apply to alpha radiation doses up to 6 Gy.

Results of preliminary analyses of lung cancer risks in dogs exposed once by inhalation to $^{239}PuO_2$ aerosols at ITRI were also provided by Hahn *et al.* (1992). Lifetime risks of lung carcinoma were calculated using a proportional hazard rate model. The dose-response curve was assumed to be linear at low doses. This yielded a risk coefficient for alpha-induced lung carcinoma of 2300 cancers/10^4 dog-Gy for doses less than 5 Gy. Similar preliminary analyses on ITRI studies of dogs that inhaled relatively insoluble aerosols of ^{90}Y, ^{91}Y, ^{144}Ce, or ^{90}Sr produced a risk coefficient for beta-induced lung carcinoma of 65 cancers/10^4 Gy for doses less than 50 Gy. From these side-by-side comparisons of the carcinogenic effectiveness of chronic alpha relative to beta radiation in the lung, the

RBE was estimated to be 36. In another preliminary analysis comparing the effectiveness of chronic alpha irradiation from $^{239}PuO_2$ to chronic beta irradiation from ^{91}Y in insoluble particles using low-dose linear models, Boecker *et al.* (1988) observed ratios from 10 to 18 depending on particle size. Estimates of uncertainty in the RBE values were not reported.

These current results are consistent with an earlier RBE estimate derived by the ICRP Task group on the Biological Effects of Inhaled Radionuclides. In a detailed analysis of worldwide animal data (mainly studies in rats) on radiation-induced lung cancer, the ICRP Task group concluded that, in terms of average dose to the lung, alpha radiation from inhaled radionuclides was about 30 times more effective than beta radiation in producing lung cancers (ICRP 1980).

3.2.2 Liver

Our current knowledge of radiation-induced cancer in the liver from internally deposited alpha-emitting radionuclides is based on direct results from long-term studies of human populations and laboratory animals that received relatively large intrahepatic deposits of alpha- or beta-emitting radionuclides.

3.2.2.1 Data from Human Populations

The major sources of information from human populations dealing with the carcinogenic effects of ionizing radiation on the liver are the follow-up studies of patients who received an intravascular injection of Thorotrast, an X-ray contrast medium containing colloidal $^{232}ThO_2$. Patients in Germany, Portugal, Japan, Denmark, and the United States have been followed for many years after the Thorotrast injections to examine the occurrence of liver cancers. Increases have been noted, particularly in the numbers of observed angiosarcomas, bile duct carcinomas, and hepatic-cell carcinomas. The BEIR IV Report (NAS/NRC, 1988) presents additional review and analysis of the data available from these five populations. Using an assumed latent period of 20 years, a linear estimate was made of the lifetime risk coefficient for liver cancer in the German patients of 300 excess cancers per 10^4 person Gy of alpha radiation to the liver. This estimate was the basis for the assessment made in ICRP Publication 60 (ICRP, 1991) and Addendum 1 (NRC, 1991). Similar lifetime risks were computed for the patients in the Japanese and Danish studies. If a latent period of 10 years was to be used instead of 20 years, the estimated risk coefficients would be reduced by about one-third.

These populations of patients injected for medical purposes with Thorotrast are the only source of human dose-response information for chronic alpha irradiation of the liver. When applying this risk coefficient to estimate the risks of liver cancer from other alpha-emitting radionuclides, it is important to remember that these liver cancers resulted from Thorotrast, a material that was colloidal in nature and contained other chemicals in addition to the $^{232}ThO_2$. These factors might result in different risk coefficients than those for other alpha-emitting radionuclides deposited more uniformly in the liver without the presence of other chemicals. However, Taylor *et al.* (1986) reported on a study in which the liver carcinogenicities of injected ^{241}Am and Thorotrast were compared using both grasshopper mice and deer mice. Because the observed liver carcinogenicity was approximately equal for equal absorbed doses, these results indicate that non-radiation factors may not play an important role in the production of liver cancers by Thorotrast.

3.2.2.2 Studies in Laboratory Animals

Much of our knowledge on the patterns of dose and response in the liver from transuranic radionuclides has been obtained from life-span studies in which laboratory animals inhaled or were injected with relatively soluble forms of these radionuclides. An important consideration in analyzing the results of these studies is the duration of radionuclide retention in the liver, because prolonged retention times increase the radiation doses received by the liver and increase the carcinogenic response seen in those species. For instance, liver cancers have been observed in several life-span studies in dogs, for which retention in the liver is prolonged, whereas the carcinogenic response in rat livers is much lower, presumably due to much shorter retention times and associated absorbed doses.

In a series of life-span studies in which dogs received a single inhalation exposure to monodisperse aerosols of $^{238}PuO_2$, late-occurring cancers were frequently observed in the skeleton, liver, and lungs (Gillett *et al.*, 1988). Most of the cancers found in the liver and skeleton were considered to have been induced by the ^{238}Pu that was absorbed after fractionation of the $^{238}PuO_2$ particles in the lung because of the high specific activity of the ^{238}Pu. The majority of the liver tumors were fibrosarcomas and tumors were seldom the cause of death. Results of the study by Gillett *et al.* suggest that the liver may be an important organ at risk for the development of neoplasia in humans at periods long after inhalation of high-specific-activity, alpha-emitting radionuclides.

Taylor *et al.* (1991) reported on the induction of liver tumors in dogs that received single, intravenous injections of either ^{239}Pu or ^{241}Am in a citrate buffer as young adults and were studied during their remaining life span. Bone cancers were the most frequently observed late effects, especially for dogs in the higher dose levels. At lower dose levels in both studies, liver cancers were also observed. The risk of liver cancers at the lower levels of injected ^{241}Am, where the survival times were long, exceeded the risk of bone cancers. These results provide additional support for the inclusion of liver as an organ at risk from internally deposited transuranic radionuclides.

The long life span of humans and the additional carcinogens to which the human liver can be subjected, such as alcohol, might enhance liver tumor expression above that seen in animal studies (Gillett *et al.*, 1988). Some investigators have speculated that the risk from liver tumors might exceed the risk from bone sarcomas for low-level intakes of Pu in humans (Mays *et al.*, 1970; Mays, 1982).

Muggenburg *et al.* (1986) used the carcinogenic response in livers of dogs that inhaled $^{144}CeCl_3$ or were injected with $^{137}CsCl$ to estimate a lifetime risk coefficient for liver cancer in humans from chronic beta irradiation. In these studies, primary liver cancers, mostly hemangiosarcomas, bile-duct carcinomas, and hepatocellular carcinomas, were the prominent long-term findings. The lifetime risk coefficient for cancer in these dogs was estimated to be 90 liver cancers per 10^4 dog-Gy. Using this value and specific assumptions related to extrapolating risk of liver cancer in dogs to the corresponding risk in people from chronic alpha irradiation, Muggenburg *et al.* estimated the lifetime risk coefficient to humans from chronic beta radiation to be 30 liver cancers per 10^4 person-Gy. It was assumed that radiation sensitivity was independent of dose rate and age of the dog and that lifetime risk per unit dose was the same in people and dogs.

Another approach to studying the relative effectiveness of alpha radiation for inducing stochastic effects in the liver has been the study of chromosome aberrations. Monomeric ^{239}Pu, ^{241}Am, and ^{144}Ce, injected in a citrate solution, were deposited relatively uniformly throughout the livers of Chinese hamsters. Alpha particles from ^{239}Pu and ^{241}Am were reported to be about 15 to 20 times more effective than protracted, low-LET radiation from ^{144}Ce in producing chromosome aberrations in Chinese hamster livers (Brooks *et al.* 1972; Brooks 1975).

3.2.3 Skeleton

3.2.3.1 Data from Human Populations

Our knowledge of the late somatic effects of alpha-emitting radionuclides in the skeleton comes mainly from studies of two populations. The first population comprises persons who obtained internal depositions of $^{226,228}Ra$ medically or occupationally as luminous dial painters or Ra chemists. The second population comprises persons treated medically with ^{224}Ra for bone tuberculosis or ankylosing spondylitis.

The $^{226,228}Ra$ studies, which have been in progress for over 60 years, have provided a wealth of information on the carcinogenic response of the skeleton to chronic, high-LET irradiation from alpha particles. The current status of these studies, involving about 2,500 persons whose doses from radium have been estimated, was reviewed in BEIR IV (NAS/NRC, 1988). This review included a discussion of the inherent difficulties associated with trying to derive a relationship between dose and response for bone cancers in persons whose skeletons received chronic alpha irradiation protracted over many years from internal deposits of $^{226,228}Ra$. These difficulties included how best to describe the dose received, whether the dose-response relationship was linear or non-linear, and whether it had a threshold. The information presented includes reviews of previous analyses by Evans *et al.* (1972) and Rowland *et al.* (1978) that demonstrated a non-linear shape of the dose-response curve and absence of bone tumors in the lower dose region. Bone sarcomas induced by $^{226,228}Ra$ appeared about 7 years after first exposure and continued to appear throughout life (NAS/NRC, 1988). The time to tumor appearance was inversely related to dose and dose rate. For absorbed skeletal doses below 0.8 Gy, the chance of developing bone cancer from $^{226,228}Ra$ was judged by the BEIR IV Committee to be extremely small and possibly zero. These factors make it difficult to describe the risk coefficient for alpha-induced bone cancer as a single number.

Results of studies of the adults and children given ^{224}Ra for treatment of ankylosing spondylitis have been given by Spiess and co-workers (Mays and Spiess, 1984; Mays *et al.*, 1986; Spiess *et al.*, 1989), and these studies are also summarized in BEIR IV (NAS/NRC, 1988). Because the radioactive half life of ^{224}Ra is only 3.6 days, the total dose to skeleton from a given skeletal deposition was delivered within about 1 month, in sharp contrast to the situation for ^{226}Ra with a radioactive half life of about 1600 years. Because of its short radioactive halflife, ^{224}Ra delivers its alpha dose primarily to the sites of initial deposition in the skeleton, bone surfaces. In contrast, $^{226,228}Ra$ is redistributed to the bone volume where it delivers most of its alpha dose.

In the persons who were treated with ^{224}Ra, bone cancers have been seen at times ranging from about 3.5 to 25 years after the initial exposure, with a peak in the occurrences at about 8 years. Several different dose-response functions for the ^{224}Ra studies were discussed in the BEIR IV report along with the associated sources of uncertainty. The results presented here are based on the average dose to the skeleton, except where stated differently. In one of these analyses, bone tumor incidence data for juveniles and adults were merged and the function fitted to the data yielded an asymptotic value for the lifetime risk coefficient for bone cancer incidence from ^{224}Ra of 200 bone sarcomas per 10^4 person-Gy (Mays and Spiess, 1984). Another treatment of these data, using a life-table analysis in which juveniles and adults were treated separately, yielded risk coefficients of 188 bone sarcomas per 10^4 person-Gy for juveniles and 133 bone sarcomas per 10^4 person-Gy for adults (NAS/NRC, 1988). However, Chemelevsky *et al.* (1986) demonstrated that most if not all of the difference in radiosensitivity between juveniles and adults originally reported resulted from failure to properly account for competing risks and loss to follow-up.

Because this latter estimate for adults of 133 bone sarcomas per 10^4 person-Gy accounted for competing risks, ICRP (1991) used it along with a factor of 0.7 to convert from a risk coefficient for bone cancer incidence to a risk coefficient for bone cancer mortality of 93 cancers per 10^4 person-Gy for ^{224}Ra.

To obtain the corresponding mortality risk estimate for low-dose-rate, low-LET irradiation, this risk coefficient should first be expressed as a function of the dose to bone surfaces, rather than average dose to the skeleton, because ^{224}Ra mainly irradiates the surfaces, and because critical target cells are presumed to reside at these surfaces. One first divides by 7.5 (Puskin *et al.*, 1992) to obtain 12.4 alpha-radiation-induced, bone sarcoma deaths per 10^4 person-Gy, based on dose to the surface of bone. The corresponding low-LET estimate is 0.6 bone sarcoma deaths per 10^4 person-Gy, based on an RBE of 20 for alpha radiation and on dose to the surface of bone.

For low-LET sources that uniformly irradiate the skeleton, the risk estimate of 0.6 bone sarcoma deaths per 10^4 person-Gy would apply to both dose to the bone surface and average dose to the skeleton, assuming the critical cells reside at the surface of bone. This estimate, which is lower by a factor of 7.5 than the estimate of 4.7 bone sarcoma deaths per 10^4 person-Gy presented in Addendum 1 (NRC, 1991) based on average dose to the skeleton, accounts for systematic error in the Addendum-1 estimate. The systematic error arose because the ^{224}Ra-alpha-specific estimate of 93 bone sarcoma deaths per 10^4 person-Gy reported in ICRP 60 (ICRP, 1991), was incorrectly indicated to be based on dose to the surface of bone, but was actually based on average dose to the skeleton (Puskin *et al.*, 1992).

3.2.3.2 Studies in Laboratory Animals

A number of large life-span studies have been conducted in dogs and other species to determine dose-response relationships for bone cancers from internally deposited actinide radionuclides (Thompson and Mahaffey, 1986; NAS/NRC, 1988). The radionuclides and exposure routes studied in Beagle dogs include injected ^{226}Ra, ^{228}Ra, ^{239}Pu and ^{241}Am conducted at the University of Utah, injected ^{226}Ra at the University of California, Davis, inhaled $^{238}PuO_2$ or $^{239}Pu(NO_3)_2$ at PNL, and inhaled $^{238}PuO_2$ at ITRI. These studies have demonstrated that the probability of tumor induction for alpha irradiation of

the skeleton depends on whether the radionuclide preferentially deposits on the bone surface (surface seeker) or within its internal volume (volume seeker). Surface seekers such as isotopes of plutonium, americium, and curium, provide greater risks of bone cancer per unit dose to the skeleton than do volume seekers such as ^{226,228}Ra. Of the alpha-emitting actinides, plutonium gives the highest bone tumor risk per unit of dose to the skeleton. Animal studies have also demonstrated that monomeric plutonium deposits in larger amounts on the surface of the endosteum than polymeric plutonium, resulting in more uniform dose distribution with the monomeric form and a higher incidence of bone tumors per unit dose to the skeleton. These studies have also demonstrated that the most common radiation-induced bone tumors are sarcomas (osteosarcomas, chondrosarcomas, and fibrosarcomas).

Many of these studies are now being completed, and risk analyses for each particular set of experimental circumstances will be forthcoming. The availability of this information will facilitate individual and cross-study analyses to determine the potential impact of various dose-and-effect modifying factors on the predicted bone cancer risks for humans from internally deposited radionuclides. After discussing the metabolism and dosimetry of various transuranic radionuclides and the general potential for impact of these factors, the BEIR IV Committee used a Bayesian methodology to examine the combined results of radionuclide-induced bone cancer in humans, dogs, and rats having depositions of ^{226}Ra, ^{228}Ra, ^{238}Pu or ^{239}Pu (NAS/NRC, 1988; DuMouchel and Groër, 1989). This analysis indicated that the risk of bone cancer due to internally deposited plutonium was about 300 cases of bone cancers per 10^4 person-Gy (based on cumulative average dose to skeleton) with a 95% confidence interval of 80 to 1100 cancers per 10^4 person-Gy.

Studies in dogs have provided estimates of the RBE for alpha radiation, as contrasted to beta radiation, in inducing bone tumors when the radiation dose is protracted. Mays and Finkel (1980) reported results obtained from injection studies with the volume seekers ^{226}Ra and ^{90}Sr. The alpha emitter ^{226}Ra was used as the test radiation source and the beta emitter ^{90}Sr was used as the reference radiation source. The RBE for alpha radiation compared to beta radiation at low doses was approximately 25. Dose-response relationships for tumor induction were based on the average skeletal dose to 1 year before death, to correct for wasted dose. For ^{239}Pu, the alpha radiation RBE was found in a similar analysis based on average skeletal dose to be 17 $\pm$ 5 (Mays *et al.*, 1987). For ^{241}Am, the alpha radiation RBE relative to ^{90}Sr beta radiation was 5 $\pm$ 2 (Mays *et al.*, 1987). The variation in RBE for the different alpha-emitting radionuclides is likely related to the use of average skeletal dose instead of using local doses to bone surfaces that differ in relative magnitude among different alpha-emitting radionuclides.

3.2.4 Bone Marrow

3.2.4.1 Data from Human Populations

As described above, osteosarcoma has been the primary long-term somatic effect seen in epidemiological studies of dial painters having internal depositions of the bone volume seekers ^{226,228}Ra. In spite of some alpha irradiation of the red bone marrow in these populations, leukemia has not been observed in significant numbers as compared with the occurrence of osteosarcomas (Spiers *et al.*, 1983; Stebbings, *et al.*, 1984; NAS/NRC, 1988). This finding in US dial painters is supported by data on a population

of radium dial painters exposed to lower radiation levels in the United Kingdom (Baverstock and Papworth, 1989)

Similar results have been observed in studies of children and adults that received repeated injections of ^{224}Ra, an alpha emitter with a radioactive half-life of 3.6 days. Because of this short half-life, most of the alpha radiation is deposited on bone surfaces in a manner similar to that of a surface-seeking radionuclide such as plutonium or americium. In spite of the proximity of these bone surfaces to the outer portion of the red bone marrow, no significant excess of leukemia has been observed in a population of 900 patients who received injections of ^{224}Ra for treatment of bone tuberculosis and ankylosing spondylitis (Spiess *et al.*, 1989). Six cases of leukemia were observed when two were expected based on German Cancer Statistics, the excess has been suggested by Spiess *et al.* to be related to the use of possible leukemogenic drugs such as phenylbutazone for a pain killer.

The only human data currently indicating some leukemogenic response from an alpha-emitting radionuclide in the skeleton have come from follow-up studies of individuals who that were injected with Thorotrast. Although liver cancer has been the main late somatic effect seen in these persons, some excess leukemias have also been observed. Because of the insoluble, colloidal nature of the Thorotrast injected intravenously, most of it is deposited in the reticuloendothelial system (RES) including the bone marrow. The BEIR IV report gave a crude estimate of 50 to 60 leukemias per 10^4 person-Gy of average dose to the bone marrow for leukemia induced by thorium based on combined surveys in Germany, Portugal, and Denmark (NAS/NRC, 1988).

3.2.4.2 Studies in Laboratory Animals

The BEIR IV Committee (NAS/NRC, 1988) presented an extensive review of the late somatic effects that have been seen for transuranic radionuclides deposited internally in laboratory animals. A wide range of species differing in body size and life span (e.g., rodents, dogs, nonhuman primates) have been exposed to these radionuclides by different routes including inhalation, ingestion, and intravenous injection. Leukemogenesis from these alpha-emitting radionuclides has not been a significant finding.

It has been shown that injection of radionuclides into the bloodstream in a monomeric form leads to deposition primarily in or on the bone but not in the bone marrow (Rosenthal *et al.* 1972; Stevens *et al.* 1975). The monomeric form is the expected form in which transuranic radionuclides would be absorbed into the bloodstream from the lung, gastrointestinal tract, or intramuscular wound site. The preponderance of data from studies in laboratory animals demonstrates that these skeletal depositions do not lead to leukemia.

One exception has been the occurrence of leukemia in CBA/H mice given single or repeated injections of ^{239}Pu. This strain of mouse has been reported to generate radiation-induced myeloid leukemias at doses less than required for the maximum yield of osteosarcoma (Humphreys *et al.*, 1985). The occurrence of alpha-radiation induced leukemias in mice but not in other species of laboratory animals may reflect a higher relative degree of marrow irradiation because of differences in the size and geometry of the marrow cavity in mice brought about by their small size. For the same total dose administered,

more cases of myeloid leukemia were seen in CBA/H mice given ^{239}Pu in divided amounts than for those given the same activity in a single amount (Humphreys *et al.*, 1987). However, the observed incidence was quite small for both single and divided administrations of ^{239}Pu. Results from subsequent experiments using ^{224}Ra instead of ^{239}Pu did not confirm an inverse dose-rate effect for the induction of leukemia (Humphreys *et al.* 1989).

3.2.5 Lymph Nodes

When relatively insoluble particles of transuranic radionuclides are cleared from the lung, one pathway is by the lymphatic drainage. In this case, these particles are filtered out from the lymph at regional nodes in the pulmonary or tracheobronchial regions. Once deposited in these nodes, these alpha-emitting radionuclides are retained for prolonged periods and produce intense, very localized irradiation of the nodal tissue. Lymphocytopenia can occur as a result of irradiation of blood passing through the lung, liver, and lymph nodes but a significant risk of primary tumors in the lymph nodes has not been seen in life-span studies with laboratory animals (NAS/NRC, 1988). Therefore, no risk coefficient for lymph node cancers from alpha radiation is included in this revision.

3.3 Risk Estimates for Late Somatic Effects

3.3.1 General Approach and Summary of the Models

For estimating the risks of late-occurring somatic health effects resulting from exposure to alpha-emitting radionuclides, three types of data are relevant:

1. Data from epidemiologic studies of persons exposed to alpha-emitting radionuclides;
2. Data from experimental studies in laboratory animals; and
3. Data from epidemiologic studies of persons exposed to low-LET radiation.

Epidemiologic data on persons exposed to low-LET radiation are far more extensive than data on persons exposed to alpha radiation. For that reason, it is often necessary to modify models for low-dose rate, low-LET radiation by appropriate factors that account for the relative biological effectiveness (RBE) of alpha radiation rather than the more direct approach of using data on persons exposed to alpha-emitting radionuclides. Data from experiments in animals have been used primarily for the purpose of estimating the RBE, but also provide lifetime risk estimates that can be compared with those obtained using other approaches.

The general model for obtaining estimates of risks of lung, liver, and bone cancer from the dose received from exposure to alpha emitters is described below. Additional detail for each of the three cancer types is given in the sections that follow.

To obtain the central estimate for lung cancer, it is recommended that the estimate for dose received from low-LET radiation at low doses and dose rates (as given in Addendum 1) be multiplied by a factor of 20 to reflect the higher RBE for alpha irradiation. This approach is consistent with that used for radiation protection practice by the ICRP and NCRP in which radiation weighting factors are used in the calculation of equivalent dose to put doses of different types on a common scale. The specific choice of

a quality factor of 20 is consistent with current recommendations of the NCRP (NCRP, 1987) and ICRP (ICRP, 1991).

For liver and bone cancer, risk estimates based on human exposure to alpha emitters are available, and it is thus recommended that these estimates be used as central estimates for exposure to alpha irradiation. As discussed in Sections 3.2.2.1 and 3.2.3.1, these estimates were 300 deaths per 10^4 person-Gy for liver cancer and 13 deaths per 10^4 person-Gy for bone cancer. The liver cancer estimate served as the basis of low-LET risk estimate, and is approximately 20 times that value recommended in Addendum 1. The low-LET risk estimate for bone cancer was also obtained by dividing the high-LET risk estimate by an RBE of 20, but, unlike the estimate recommended here, was incorrectly based on average dose to the skeleton rather than dose to the bone surface (see Section 3.2.3.1).

To obtain upper and lower bound estimates for exposure to alpha-emitting radionuclides, it is recommended that the central estimates be multiplied by the ratios of the upper and lower bound estimates to the central estimate for low-LET radiation. For obtaining the numbers of excess deaths, these ratios for obtaining upper and lower bounds, respectively, are 4.2 and 0.22 for lung cancer, 2.0 and 0.20 for liver cancer, and 2.0 and 0.50 for bone cancer. For lung cancer and liver cancer, these are approximately the values that would be obtained if low-LET upper and lower bounds were multiplied by an RBE of 20.

The approach recommended above should be applied regardless of the dose or dose rate of the alpha radiation exposure.

The upper and lower bound estimates for low-LET radiation reflect uncertainty from several sources including a factor of two for the choice of dose and dose rate effectiveness factor (DDREF). The uncertainty from sources other than the choice of DDREF applies to alpha as well as low-LET radiation. For alpha radiation, it seems reasonable to also include this factor of two, but to attribute it to uncertainty regarding the shape of the dose-response functions and to uncertainty regarding the dependence of risks on factors such as the chemical and physical form of the radionuclide. For lung cancer, this factor also reflects uncertainty in the RBE, because lung cancer risk estimates were derived from studies involving low-LET radiation.

As in the models for low-LET radiation, the upper and lower bounds are intended to reflect alternative assumptions that are reasonably consistent with the data. The bounds cannot be assigned a level of confidence, and may not include all sources of uncertainty. Because the upper bounds are intentionally conservative, they should not be used or interpreted as point estimates of risk.

As with low-LET radiation, most risks are to be calculated based on the estimated average dose to various organs, including the lung, liver, and skeleton. To obtain estimates of total risk from both alpha radiation and low-LET radiation, the predicted numbers of cancers based on the two dose components should be added. This procedure can be applied to obtain central, as well as upper and lower bound, estimates.

Estimates of cancer incidence (including non-fatal cancers) in NUREG/CR-4214 (NRC, 1989a) and in Addendum 1 (NRC, 1991) made use of the ratio of U.S. age-specific incidence and mortality rates. For lung cancer, this resulted in estimates that were 11.5% higher than mortality estimates. We thus recommend increasing lung cancer mortality estimates by this amount to obtain estimates of lung cancer incidence. Addendum 1 did not address the issue of obtaining incidence estimates specifically for cancer of the liver and bone. However, ICRP (1991) recommends lethality fractions of 0.95 and 0.70, respectively, for these two cancers. Thus, to obtain incidence estimates for cancer of the liver and bone, we recommend dividing the mortality estimates by 0.95 and 0.70, respectively.

Calculation of risks from the internal deposition of alpha emitting radionuclides requires estimations of the dose received during different time periods after exposure. The description of the treatment of this exposure pathway from NUREG/CR-4214 (p.II-178) is repeated below (NRC, 1989a).

> Radioactive materials inhaled at the time of the accident will continue to decay and generate doses for years after the accident. Moreover, the age structure of the population affected will change over time. In treating such exposure, the assumption is made that all exposure received during a given decade after the accident occurs at the beginning of a particular decade. The effects of exposure occurring as a result of dose received in the n^{th} decade after the accident can be calculated by omitting persons exposed at ages less than 10n from the calculations. For example, the population receiving doses two decades after the accident from radioactive materials inhaled or ingested at the time of the accident would not include persons under 20 years of age.

A summary of the models used in Addendum 1 for estimating risks of cancer mortality and incidence resulting from exposure to low-LET radiation is provided in Tables 3.2 and 3.3. For a detailed description of the reasons these models were selected, the reader should consult Addendum 1 (NRC, 1991). The resulting central, upper, and lower bound estimates for lifetime risks of mortality resulting from exposure at low doses and dose rates are given in Table 3.4. Tables 3.3 and 3.4 have been amended from those provided in Addendum 1 to provide additional detail for liver cancer. These details are discussed in section 3.3.3. Finally, Table 3.5 shows how these estimates are modified to provide estimates for lifetime risks of mortality resulting from exposure to alpha emitters. Estimates in Tables 3.4 and 3.5 apply to a population with an exposure age and sex distribution similar to that of the U.S. population in 1978. For internally deposited alpha- and beta-emitting radionuclides, the age and sex distribution may change over time; risks for such exposure need to be calculated by considering the estimated patterns of alpha and low-LET doses over time, as described in the above insert from NUREG/CR-4214 (NRC, 1989a).

Table 3.2 (Adapted from Table 3.19 of Addendum 1; NRC, 1991)

Summary of the low-LET model used to determine upper bound, central, and lower bound lifetime risk estimate for mortality and incidence[a,b]

Effect	Risk estimate		
	Upper bound	Central	Lower bound
Cancers due to other than *in utero* exposure			
Leukemia and bone	Use absolute linear estimate	Modify upper bound by a DDREF of 2	Modify upper bound by a DDREF of 4
Breast	Use age-specific relative linear estimate	Use alternative age-specific relative linear estimate	Modify absolute linear estimate by a DDREF of 4
Lung	Use age-specific relative linear estimate	Modify alternative age-specific relative linear estimate by a DDREF of 2	Modify absolute linear estimate by a DDREF of 4
Gastrointestinal	Use age-specific relative linear estimate	Modify age-specific relative linear estimate by a DDREF of 2	Modify absolute linear estimate by a DDREF of 4
Thyroid[c]	Use age-specific absolute linear estimate	Use age-specific absolute linear estimate	Use age-specific absolute linear estimate
Skin	Use relative linear estimate	Modify upper bound by a DDREF of 2	Modify upper bound by a DDREF of 4
Other cancers	Use age-specific relative linear estimate	Modify age-specific relative linear estimate by a DDREF of 2	Modify absolute linear estimate by a DDREF of 4
Benign thyroid nodules[d]	Use age-specific absolute linear estimate	Use age-specific absolute linear estimate	Use age-specific absolute linear estimate
Cancers due to *in utero* exposure	Use absolute linear estimate	Use absolute linear estimate multiplied by 0.4	Use absolute linear estimate multiplied by 0.4

[a] The linear estimates for mortality are given in Table 3.4.

[b] For convenience, "linear lifetime risk estimates based on the absolute (relative) risk model" are referred to as "absolute (relative) linear estimates."

[c] ^{131}I is assumed to be as effective as external radiation for the upper bound thyroid cancer risk estimate, one third as effective for the central estimate, and one tenth as effective for the lower bound.

[d] ^{131}I is assumed to be as effective as external radiation for the upper bound thyroid nodules risk estimate, and one fifth as effective for the central estimate and lower bound.

Table 3.3 (Adapted from Table 3.20 of Addendum 1; NRC, 1991)

Risk coefficients and lifetime risk estimates for mortality from several cancer types for exposure to low-LET radiation

Effect	Period at risk (yrs)	Risk coefficient		Number of deaths[a] (per 10^4 person-Gy)		Years of life lost[a] (per person-Gy)	
		Absolute (per 10^4 PYGy)	Relative (per Gy)	Absolute	Relative	Absolute	Relative
Leukemia	2-27	4.5	—	97	—	0.34	—
In utero[b]	0-12	25[c]	—	3[d]	—	0.02	—
Bone cancer[e]	2-27	0.05	—	1	—	0.004	—
Breast cancer							
Age-specific[f]	10-life	—	1.0[h],0.4[h]	—	84[i]	—	0.14[i]
Alternative age-specific[g]	10-life	—	0.7[h],0.3[h],0.1[h]	—	54[i]	—	0.09[i]
Non-age-specific	10-life	2.6	—	43[i]	—	0.1[i]	—
Lung cancer							
Age-specific[f]	10-life	—	1.5[h],0.5[h]	—	331	—	0.49
Alternative age-specific[g]	10-life	—	0.6[h],0.3[h]	—	155	—	0.23
Non-age-specific	10-life	2.5	—	67	—	0.12	—
Gastrointestinal cancer[j]							
Age-specific	10-life	—	1.2[h],0.4[h]	—	336	—	0.41
Non-age-specific	10-life	4.0	—	135	—	0.33	—
Thyroid cancer[k]	5-life	0.25[h],0.12[h]	—	7	—	0.02	—

(concluded on next page)

Table 3.3 (Adapted from Table 3.20 of Addendum 1; NRC, 1991) (concluded)

Risk coefficients and lifetime risk estimates for mortality from several cancer types for exposure to low-LET radiation

Effect	Period at risk (yrs)	Risk coefficient		Number of deaths[a] (per 10^4 person-Gy)		Years of life lost[a] (per person-Gy)	
		Absolute (per 10^4 PYGy)	Relative (per Gy)	Absolute	Relative	Absolute	Relative
Liver Cancer							
Age-specific	10-life	—	1.2[h,l],0.4[h,l]	—	33.6	—	0.04
Non-age-specific	10-life	0.4[l]	—	13.5	—	0.03	—
Other Cancer							
Age-specific	10-life	—	1.1[h],0.25[h]	—	276	—	0.38
Non-age-specific	10-life	3.5	—	118	—	0.29	—
In utero[b]	0-12	28[c]	—	3[d]	—	0.02	—

[a] These risks are based on a linear model and in most cases must be modified as indicated in Table 3.2 to obtain central and lower estimates.
[b] These estimates may be too high because of recent improvements in cure rates. See Section 3.3.3 of NUREG/CR-4214; NRC, 1989a.
[c] These coefficients apply to the *in utero* population only.
[d] These lifetime risk estimates apply to the entire population and are 1 percent of the risks for the *in utero* population.
[e] Risk estimates in Addendum 1 (NRC, 1991) were reduced by a factor of 7.5 (Puskin *et al.*, 1992) to correct for a systematic error in the dosimetry associated with the risk coefficient for ^{224}Ra alpha-radiation-induced bone cancer presented in ICRP Publication 60 (ICRP, 1991).
[f] These age-specific estimates are used to obtain upper bound estimates.
[g] These alternative age-specific estimates are used to obtain central estimates.
[h] In each case, the first coefficient applies to those under age 20 at exposure and the second coefficient applies to those 20 and over at exposure. For breast cancer, the three coefficients are for those exposed under age 20, 20-39, and ages 40 and over.
[i] These lifetime risk estimates apply to the entire population and are one-half the risks for females.
[j] The allocation of GI cancer risk among the specific organs is discussed in Addendum 1, Section 3.4.5. (NRC, 1991). Liver cancer is included in these values.
[k] Thyroid cancer mortality risk coefficients have been obtained by reducing the incidence coefficients given in Table 3.21 of Addendum 1 by a factor of ten (NRC, 1991). See Section 3.3.3 and 2.6 of NUREG/CR-4214 (NRC, 1989a).
[l] These coefficients are applied to gastrointestinal death rates for the U.S. reduced by a factor of 10; the factor of 10 was obtained by consideration of Thorotrast data on liver cancer risks (Addendum 1, Section 3.4.5) (NRC, 1991).

Table 3.4 (Adapted from Table 3.22 of Addendum 1; NRC, 1991)

Central, upper, and lower estimates for lifetime risks of mortality resulting from low-LET exposure received at low doses (<0.2 Gy) or low dose rates (<0.1 Gy per hour)

Type of fatal cancer	Number of deaths (per 10^4 person-Gy)			Years of life lost (per person-Gy)		
	Lower bound[a]	Central estimate[b,c]	Upper bound[c,d]	Lower bound[a]	Central estimate[b,c]	Upper bound[c,d]
Cancers due to other than *in utero* exposure						
Leukemia	24	49	97	0.08	0.17	0.34
Bone[e]	0.3	0.6	1.2	0.001	0.002	0.004
Breast	11	54	84	0.02	0.09	0.14
Lung	17	78	331	0.03	0.11	0.49
Gastrointestinal[f]	34	168	336	0.08	0.20	0.41
Thyroid	7.2	7.2	7.2	0.02	0.02	0.02
Other	30	138	276	0.07	0.19	0.38
Total[g]	126	499	1,140	0.31	0.80	1.81
Liver[h]	3.4	16.8	33.6	0.008	0.02	0.04

(concluded on next page)

Table 3.4 (Adapted from Table 3.22 of Addendum 1; NRC, 1991) (concluded)

Central, upper, and lower estimates for lifetime risks of mortality resulting from low-LET exposure received at low doses (<0.2 Gy) or low dose rates (<0.1 Gy per hour)

Type of fatal cancer	Number of deaths (per 10^4 person-Gy)			Years of life lost (per person-Gy)		
	Lower bound[a]	Central estimate[b,c]	Upper bound[c,d]	Lower bound[a]	Central estimate[b,c]	Upper bound[c,d]
Cancers due to *in utero* exposure						
Leukemia	1.2[i]	1.2[i]	3.0	0.008[i]	0.008[i]	0.02
Other	1.2[i]	1.2[i]	3.0	0.008[i]	0.008[i]	0.02

[a] With the exception of thyroid cancer and cancers resulting from *in utero* exposure, these estimates are obtained by modifying the absolute linear estimates in Table 3.3 by a DDREF of 4.

[b] With the exception of breast cancer, thyroid cancer and cancers resulting from *in utero* exposure, these estimates are obtained by modifying linear estimates in Table 3.3 by a DDREF of 2.

[c] Central estimates and upper bounds for leukemia, bone, and thyroid cancer are based on the absolute risk model, while central estimates and upper bounds for remaining cancers are based on the relative risk model.

[d] These estimates are unmodified age-at-exposure-specific (except for leukemia and bone cancer) linear estimates.

[e] Risk estimates in Addendum 1 (NRC, 1991) were reduced by a factor of 7.5 (Puskin *et al.*, 1992) to correct for a systematic error in the dosimetry associated with the risk coefficient for ^{224}Ra alpha-radiation-induced bone cancer presented in ICRP Publication 60 (ICRP, 1991). These risk factors are based on dose to bone surfaces.

[f] The allocation of GI cancer risk among the specific organs is discussed in Addendum 1, Section 3.4.5. (NRC, 1991).

[g] These are the totals that would be obtained if all organs received the same dose.

[h] These coefficients are applied to gastrointestinal death rates for the U.S. reduced by a factor of 10; the factor of 10 was obtained by consideration of thorotrast data on liver cancer risks (Addendum 1, Section 3.4.5) (NRC, 1991).

[i] These estimates are obtained by modifying the upper bound estimates by 0.4 (see Section 3.4.9 of NUREG/CR-4214; NRC, 1989a).

Table 3.5

Central, upper, and lower estimates for lifetime risk of mortality resulting from exposure to alpha radiation[a]

Type of fatal cancer	Number of deaths (per 10^4 person-Gy)			Years of life lost (per person-Gy)		
	Lower bound	Central estimate	Upper bound	Lower bound	Central estimate	Upper bound
Lung[b]	350	1600	6700	0.62	2.3	9.8
Liver[c]	60	300	600	0.15	0.36	0.72
Bone[d]	6	12	24	0.02	0.04	0.08

[a] Risk estimates applicable to populations with similar age structure and male to female ratio as U.S. Population. Uncertainty in central risk estimates presumed to be accounted for by judgmental bounds provided.

[b] Risk estimates derived using average dose to lung. For transuranic radionuclides that deposit in the pulmonary region, average dose to lung should also be used. Estimates based on extrapolation from A-bomb survivor data.

[c] Risk estimates derived using average dose to liver. Estimates based on Thorotrast epidemiological studies.

[d] Risk estimates derived using endosteal dose to skeleton based on ^{224}Ra epidemiological studies (Puskin *et al.*, 1992).

3.3.2 Risk Estimates for Lung Cancer

Risk estimates for lung cancer resulting from exposure to alpha emitters are obtained from the low-LET models by multiplying the central estimates and upper and lower bounds for exposure at low dose rates by a factor of 20. The low-LET lung cancer risk model provided in Addendum 1 was based on A-bomb survivors exposed at high dose rates, primarily to low-LET radiation. Several problems needed to be addressed in developing this model, including the method of projecting risks over time (some studies have indicated a decline in the excess relative risk with time since exposure), the method of transporting risks from the Japanese to the U.S. population (baseline lung cancer risks are larger in the U.S. than in Japan), and the treatment of age at exposure (nearly all other types of cancer show strong evidence of larger risks for those exposed early in life, but evidence for such an effect for lung cancer is limited). The upper and lower bounds for lung cancer risks reflect uncertainties from these sources as well as uncertainty in the choice of DDREF. The lung cancer model for low-LET radiation is summarized in Tables 3.2, 3.3, and 3.4.

Uncertainty regarding the modifying effects of time since exposure, population (Japan versus U.S.), and age at exposure applies to exposure from alpha radiations as well as to low-LET radiations. In the absence of direct data on these factors for alpha radiation, handling these uncertainty sources in the same manner as for low-LET radiation seems reasonable.

The uncertainty in the choice of DDREF does not apply, but the alpha radiation models nevertheless include this additional factor of two. For lung cancer risks, this additional uncertainty includes uncertainty in the estimated RBE as well as other uncertainties. Although the value 20 is reasonably consistent with experimental evidence, some studies have suggested larger values. On the other hand, the central estimate for lung cancer of about 1600 deaths per 10^4 person-Gy (Table 3.5) agrees with the estimate obtained by using model 4(b) and 5 mGy/WLM in Table 3.1. However, this estimate is at the upper end of the range of risk estimates obtained from studies of underground miners (Table 3.1), and this might suggest a lower value. However, uncertainty in the appropriate factor for converting WLM to Gy makes such comparisons imprecise.

The highest risk estimate obtained through linear extrapolation from the animal studies presented here, involving exposure to inhaled plutonium, was 2300 per 10^4 person-Gy, suggesting that the upper limit of 6700 per 10^4 person-Gy may be overly conservative. However, the absence of human data on such exposure and the absence of adequate information on the possible modifying effects of the chemical and physical form of the radiation would seem to justify allowing a large measure of uncertainty. Some experimental studies with plutonium, for instance, have indicated dependence on the isotopic form and physicochemical forms (Dagle *et al.*, 1989), and some analyses of experimental data have indicated response functions that are distinctly non-linear.

Recently, it has been suggested that the neutron dose in Hiroshima may have been significantly underestimated (Straume *et al.*, 1992). If this is the case, then risk estimates based on the A-bomb survivor data (as used in Addendum 1; NRC, 1991) may be too large. Risk models for both alpha and low-LET radiation could possibly need modification if further re-evaluation of neutron dosimetry bears out preliminary results. For alpha radiation, only lung cancer risks would be affected.

3.3.3 Risk Estimates for Liver Cancer

Addendum 1 (NRC, 1991) provided a model for all gastrointestinal cancers, but did not give detailed attention to liver cancer. However, in section 3.4.5 of Addendum 1, it was noted that by reducing the risk estimate obtained from Thorotrast studies by an assumed RBE of 20, a central estimate of 15 deaths per 10^4 person-Gy would be obtained. Because this estimate is about 10% of the central estimate for gastrointestinal cancers (168 per 10^4 person-Gy), it was suggested that for the percentage allocation among specific cancers, 10% of the gastrointestinal cancer risk be attributed to liver cancer, thus yielding a similar estimate (16.8 per 10^4 person-Gy) to the estimate from the thorotrast patients by an RBE of 20 (15 per 10^4 person-Gy). Upper- and lower-bound estimates for liver cancer estimates for low-LET were obtained by reducing the comparable upper and lower bound estimates for all gastrointestinal cancer by 10%.

For estimating effects of high-LET radiation, it seems more sensible to retain the original estimate of 300 deaths per 10^4 person-Gy obtained from the Thorotrast patients as the central estimate for liver cancer. To obtain upper and lower bound estimates, we recommend multiplying this estimate by the ratios of the upper- and lower-bound estimates to the central estimate for gastrointestinal cancers induced by low-LET radiation. For obtaining numbers of excess deaths, these ratios are 2.0 and 0.20 for upper and lower bounds, respectively.

The central and upper bound estimates for gastrointestinal cancers for low-LET radiation were based on the relative risk projection model, and the projection of risks over time involved the use of age-specific rates for all gastrointestinal cancers. It might be argued that for determining the pattern of risks over time (needed for calculating the number of life-years-lost), age-specific liver cancer rates should be used for obtaining estimates of liver cancer risks. However, because the degree of increase with age for liver cancer is similar to that for all gastrointestinal cancers, we do not think this refinement is necessary. The lower bound estimate for gastrointestinal cancers was based on an absolute risk model for projecting risks over time.

As described above, the low-LET liver cancer model includes uncertainty regarding the method for projecting risks over time, and uncertainty in the DDREF. The uncertainty in the method of projecting risks over time is preserved in the model for alpha radiation, but the DDREF does not apply. However, this factor of two is retained to account for other uncertainties that include the shape of the dose-response function and the use of Thorotrast data for evaluating risk from transuranics such as americium, curium, and plutonium.

3.3.4 Risk Estimates for Bone Cancer

The central estimate for bone cancer resulting from low-LET radiation exposure at low doses and dose rates given in Addendum 1 (NRC, 1991) was obtained by reducing a lifetime risk estimate of 97 per 10^4 person-Gy based on chronic alpha irradiation data by an assumed RBE of 20. For estimating the effects of alpha radiation on the skeleton, this estimate, derived from persons injected with ^{224}Ra, will be retained as the central estimate for bone cancer based on the average skeletal dose. However, as discussed in Section 3.2.3.1, if this estimate is to be appropriately based on dose to the endosteal bone surfaces, it needs to be divided by 7.5. Thus, a lifetime risk estimate of 12 per 10^4 person-Gy is recommended as the central estimate for bone cancer resulting from exposure to alpha irradiation when dose to bone surfaces is used. Other features of the low-LET model are retained. A model in which the absolute risk was assumed to be constant for 2-27 years following exposure was assumed to determine the distribution of risk over time. A factor of two was used to obtain upper and lower bound estimates, reflecting uncertainty in the DDREF. For alpha radiation, this uncertainty can be attributed to uncertainty regarding the shape of the dose-response function, uncertainty regarding dosimetry for estimating the average dose to bone tissue or endosteum in epidemiologic studies, and uncertainty regarding the modifying effects of dose rate patterns and spatial distribution of dose.

3.3.5 Risk Estimates for Leukemia

The use of an RBE of 20 to relate the risks of late somatic effects from low-LET and high-LET radiations does not provide meaningful risk estimates for leukemia from high-LET irradiation. Multiplying the central risk estimate for leukemia from low-LET radiation given in Table 3.3 by an RBE of 20 would provide an estimated risk for leukemia of 980 leukemia deaths per 10^4 person-Gy for alpha radiation, a value that is clearly much higher than values from studies in either human subjects or laboratory animals.

The lack of a leukemogenic response seen after most exposures to bone-seeking transuranic radionuclides was noted in BEIR IV (NAS/NRC, 1988) and other sources. Priest (1989) presented a detailed analysis of the possible risks of leukemogenesis under these circumstances. He concluded that neither bone-volume or bone-surface deposition of a transuranic radionuclide would produce a significant leukemogenic irradiation of bone marrow because of the size of the marrow volume and the short range of alpha radiations. He did note the possibility of a more leukemogenically effective irradiation of bone marrow by ^{239}Pu translocated there in macrophages as a result of long-term bone remodeling processes. In this latter case, the foci of ^{239}Pu might be distributed throughout the bone marrow.

Because only a fraction of an inhaled transuranic radionuclide is translocated from the lung, especially for the relatively insoluble forms expected to be released from a nuclear power plan accident, and only a fraction of that translocated reaches the skeleton, the fraction reaching the bone marrow should represent only a very small part of the initial lung burden. Unless there is compelling evidence for a specific pattern of leukemogenic bone marrow irradiation (e.g., Thorotrast cases), consideration of the late somatic effects in lung, liver, and skeleton should provide ample consideration of alpha-radiation effects in the NUREG/CR-4214 models (NRC, 1989a, 1991). Therefore, no risk coefficient for leukemia induced by alpha radiation is included in this revision of these NUREG/CR-4214 models.

3.4 Summary

Considering inhalation to be the major mode of exposure to alpha radiation, and using results from dosimetry studies in animals, it was concluded that the critical targets for late somatic effects of alpha irradiation are the lung, liver, and bone. Available epidemiological and animal data on the carcinogenic effects of alpha irradiation were reviewed. Based on these reviews, additional refinements in NUREG/CR-4214 (NRC, 1989a) models are recommended, beyond those in Addendum 1 (NRC, 1991). Specifically, it is recommended that the alpha and low-LET, radiation-associated risks be evaluated separately, then added. The low-LET contribution to the overall risk for a specific type of cancer should be evaluated using the models presented in Addendum 1 including a DDREF of 2. Risk estimates for low-LET radiations are reproduced in Tables 3.2, 3.3, and 3.4 for convenience of the user. Risk estimates for alpha radiation recommended for use in the NUREG/CR-4214 models, based on currently available information on these risks, are given in Table 3.5 along with recommended judgmental values for upper and lower bounds that reflect uncertainties in the DDREF for low-LET radiation, the RBE for chronic alpha vs. chronic beta radiation, extrapolation of data from laboratory animals to humans, and a number of other factors.

4.0 GENETIC EFFECTS

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4.1 Introduction

Estimation of the numbers of cases of genetically related ill health as a result of human population exposure to alpha-emitting radionuclides released during a nuclear reactor accident involves much greater uncertainty than estimating those cases expected from the low-LET exposures, as addressed in NUREG/CR-4214 (NRC, 1989a) and its Addendum 1 (NRC, 1991). There are several reasons for this uncertainty. First, there are no human data. To a somewhat lesser extent, this is also true in the case of low-LET radiation. The genetic studies done on offspring of exposed survivors of the atomic bombings of Hiroshima and Nagasaki, while not yielding definitive data, at least allow estimates to be made of the upper limit of these effects and therefore of the lower limit of doubling dose, but these are for the low-LET component of dose. The high-LET component of dose was much smaller and, in any case, composed almost entirely of neutrons, not the alpha particles of interest here (RERF, 1987). Thus, even greater reliance must be placed upon data from laboratory animals, particularly the mouse, than is the case for low-LET radiations.

Second, the available experimental data on genetic effects of alpha radiation are sparse. Most of the experimental research done on genetic effects of high-LET radiations has, for reasons of convenience, particle penetration, and ease of dosimetry, been done with fast neutrons, or, for cellular systems, with accelerator-derived protons. While general principles can be derived from such studies (see NCRP, 1990 for a recent review), their results do not allow straightforward prediction of genetic effects of alpha radiation.

Finally, dosimetry for genetic effects in mammals induced by exposure is exceedingly difficult. The genetic effects resulting from human exposure to alpha radiation as a result of a nuclear power plant accident will come exclusively from alpha-emitting radionuclides incorporated into the body. Because of the extremely short range of alpha particles in tissues, only that fraction of body burden actually incorporated into the gonads has any genetic effect. For the same reason, local inhomogeneity in radionuclide distribution leads to great inhomogeneity in absorbed dose on a microscopic scale. Interspecies differences in gonadal architecture thus lead to large differences in genetic response to a given gonadal radionuclide burden. Interspecies differences in radionuclide absorption, translocation, and clearance further complicate genetically effective dose determination.

Given accurate, genetically significant, dose estimates, the question of numbers of genetic effects to be expected as a result of exposure of human gonads to alpha radiation is basically one of RBE. As with other effects, however, application of simple RBE values is complicated by changes in dose and in dose rate. For genetic effects, RBE is not single-valued, but rather a function of dose rate. RBE may, however, be single-valued at sufficiently low-dose rate.

The BEIR IV report (NAS/NRC, 1988) provided specific estimates of the numbers of genetic effects to be expected as a result of human population exposure to internally deposited alpha-emitting radionuclides. The objective of this chapter is to incorporate these estimates with other evidence into the NUREG/CR-4214 (NRC, 1989a) health effects models so that the contribution of alpha radiation can be included in estimates of genetic-effects consequences of an accident at a nuclear power plant. First, it is necessary to review some of the general radiobiological principles derived from experimental studies.

4.2 Radiobiological Considerations

The literature on the relative biological effectiveness of radiations of different quality has recently been extensively reviewed (NCRP, 1990). Only the general principles involved in incorporating estimates of alpha-radiation-induced genetic effects into the health effects models will be outlined here.

4.2.1 Dose-Effect Curves

Although dose-effect curves for the induction of mutations by acute doses of low-LET radiations such as gamma and X rays were long believed to be essentially linear, recent evidence has shown that they are "superlinear," following a quadratic (so-called linear-quadratic) expression (neglecting high-dose saturation):

$$Y = a + \alpha D + \beta D^2,$$

where Y is yield, a is the spontaneous frequency, α is the coefficient for the fraction arising as a linear function of dose (D), and β is the coefficient for the fraction arising as a function of the square of the dose. Thus, αD gives the "one-hit" component, and βD^2 gives the "two-hit" component. Abrahamson and Wolff (1976) have shown this to be the case for mutation in the mouse and Abrahamson *et al.* (1981) for Drosophila oogonia. This consideration was incorporated into the genetic-effects model in NUREG/CR-4214 (NRC, 1989a).

It is obvious that the two-hit component contributes little to overall yield if dose is very low (the contributions from one- and two-hit events only reach equality at a dose of α/β, generally taken to be of the order of 0.5 to 1.0 Gy for mammalian cells). In NUREG/CR-4214 (NRC, 1989a), the value of β was taken to be zero below 0.5 Gy, and the complete linear-quadratic expression was used only for acute exposures above 0.5 Gy.

For high-LET irradiations, however, dose-effect curves are clearly linear (again neglecting saturation). Thus, they display only an α slope, with no β component. For this reason, RBE depends upon dose when the low-LET reference dose is acute, increasing with decreasing dose and approaching a limiting value (the "ultimate" RBE of Neary *et al.*, 1961, or RBE_M of ICRP, 1963), as the value of β approaches zero, where the RBE becomes simply the ratio of the α slopes for the radiation qualities.

4.2.2 Dose Rate

Linear-quadratic dose-effect curves observed for acute doses of low-LET radiation are influenced by dose rate as this rate decreases from the acute into the chronic range. What is observed experimentally is that the value of β decreases with decreasing dose rate, eventually becoming zero at a low enough dose rate, while the value of α does not change with dose rate. Thus, the low-LET dose-effect curve becomes

linear at low-dose rate. In NUREG/CR-4214 (NRC, 1989a), this dose-rate effect was allowed for by the use of only the α component for doses below 0.5 Gy, because below this dose, the yields expected are independent of dose rate. The linear dose-effect curves observed for genetic effects induced by high-LET radiations, on the other hand, generally are influenced little, if at all, by dose rate.

4.2.3 Relative Effectiveness and LET

The biological effectiveness of high-LET radiation per unit dose is generally greater than that of low-LET radiation, i.e. RBE > 1. As a rule, effectiveness rises to a maximum at an LET of about 100 keV/μm (track average), depending on the system being observed, then begins to decrease at even higher LET. Up to values on the order of 100 keV/μm, then, RBE is always greater than unity. An exception occurs in comparisons where the low-LET curve is supralinear and the two dose-effect curves "cross over" at some high value of dose, above which the high-LET radiation is actually less effective than the low-LET. This "humped" relation of biological effectiveness to LET is important to note because it explains the otherwise puzzling observation that alpha radiation often displays lower empirical values of RBE than do radiations of lower LET, such as the often-studied fast neutrons, despite the fact that they are also high-LET radiations.

4.3 Genetic Effects Estimates

Addendum 1 to NUREG/CR-4214 (NRC, 1991) revised the earlier genetic effects models in light of new estimates given in BEIR V (NAS/NRC, 1990), UNSCEAR, 1986; UNSCEAR, 1988; ICRP Publication 60 (ICRP, 1991), and other recent information. The recommended new estimates are presented in Table 4.1 of Addendum 1. After consideration of the scanty information available on mutations and chromosomal aberrations induced in the laboratory mouse by internally deposited, alpha-emitting radionuclides, estimates were given in the BEIR IV report (NAS/NRC, 1988) of the genetic effects to be expected in consequence of human population exposure to such alpha particle emitters. Adopting the BEIR IV values, we have used the NUREG/CR-4214 (NRC, 1989a) genetic effects models to estimate the components of genetic effect to be anticipated as a result of exposures to alpha particle emitters resulting from accidents in nuclear power plants. For easy comparison with other NUREG/CR-4214 estimates, Table 4.1 compares BEIR V-derived estimates with those recommended below in the same format used in Table 4.1 of Addendum 1.

4.3.1 Experimental Basis

The experimental evidence reviewed by the BEIR IV committee consisted largely of specific locus and dominant lethal, mutations and chromosomal aberration tests on male mice injected with ^{239}Pu (NAS/NRC, 1988). For specific locus mutations, the estimated RBE reported was about 2.5. For dominant lethal mutations, believed to result largely from chromosomal aberrations, and for chromosomal aberrations, the estimated RBEs ranged from 10 to 20. BEIR IV adopted the values of 2.5 for all mutations, and 15 for chromosomal aberrations. Though the experimental evidence was limited to exposure of male mice, these values were adopted for exposure of females as well.

Table 4.1

Numbers of naturally occurring and radiation-induced (low- and high-LET) genetic disorders in a population of 1 million, according to the BEIR IV and BEIR V reports and the present analysis. Assumes a 0.01 Gy gonad alpha radiation dose. (Derived from Table 4.1, Addendum 1 [NRC, 1991])

	Low-LET chronic[a] Addendum 1			Alpha radiation[a] (this report)	
Type of disorder	Normal incidence[b]	First generation	All generations	First generation	All generations[c]
Single-gene					
- Dominant	4,800	15	70	40	175
- X-linked	190	4	20	10	50
Chromosome aberrations					
- Aneuploidy	1,830	4	5	10	15
- Unbalanced translocations	290	6	8	90	120
Congenital abnormalities	11,800	-	15	--	40
TOTALS[c]	18,900	30	120	150	400
Periimplantation wastage	260,000	230	240	1,300	1,350

[a] Central estimates. Guidance for calculation of minimum and maximum estimates given in NUREG/CR-4214 (NRC, 1989a). Numbers of cases expected among offspring of population of 10^6 persons each receiving a gonadal dose of 0.01 Gy of alpha particles. Assumes 30 years intergenerational interval and birthrate of 16,000 per year per 10^6 persons.

[b] For a total population of 10^6 persons (16,000 live births per year) for 30 years (480,000 live births). New estimates for Addendum 1 based upon BEIR V estimate (NAS/NRC, 1990).

[c] Total rounded to avoid unduly implying great precision.

4.3.2 Autosomal Dominants and X-linked Mutations

Application of the recommended RBE of 2.5 to the central estimates in NUREG/CR-4214 (NRC, 1989a) for chronic low-LET radiation exposure, 15 dominants in the first generation and 70 over all generations following exposure of a population of 1 million to 0.01 Gy, yields estimates of 38 in the first generation and 175 over all time for exposure to alpha radiation. Similarly, the central estimates for chronic low-LET of 4 and 20 for x-linked mutations become 10 and 50 for the first generation and over all generations, respectively, for exposure to alpha radiation. These estimates are to be applied independently of any consideration of dose rate.

4.3.3 Aneuploidy

Because no numerical estimate for aneuploidy was made in the BEIR III report (NAS/NRC, 1980), the BEIR IV Committee recommended no RBE factor for this class of effect. Indeed, no empirical evidence is available upon which to base an estimate. The induction of aneuploidy or, more properly, nondisjunction that gives rise to aneuploid gametes, by radiation is not well understood, but could arise through alteration of the DNA in the centromeric region of a chromosome. This would be a mutational event as usually defined, not a gross chromosomal aberration. We recommend, though an arbitrary choice, that the gene mutation RBE factor of 2.5 be applied for aneuploidy induction by α particle irradiation of the gonads. Thus, the Addendum 1 (NRC, 1991) estimates for the first generation and all generations of 4 and 5 become 10 and 13, respectively, for a population of 1 million exposed to a gonadal dose of 0.01 Gy of alpha radiation.

4.3.4 Unbalanced Translocations

When the RBE factor of 15 recommended in the BEIR IV report (NAS/NRC, 1988) is applied to the Addendum 1 (NRC, 1991) estimates for chronic irradiation of 6 in the first generation and 8 over all generations, the values become 90 in the first generation and 120 over all generations following exposure of a population of 1 million to 0.01 Gy of gonad dose from alpha radiation.

4.3.5 Irregularly Inherited

Addendum 1 (NRC, 1991), based upon the BEIR V committee precedent (NAS/NRC, 1990), made separate estimates for the sub-class of congenital abnormalities other than those caused by chromosomal aneuploidy.

The BEIR IV report (NAS/NRC, 1988) applied the RBE derived from specific-locus-mutation information, 2.5, to the category of irregularly inherited genetic effects, assuming them to result from interactions of independent gene mutations. Assuming this to be the case for congenital abnormalities (other than those expressed in the first generation, which are by definition dominant), the Addendum 1 central estimate of 15 cases over all generations becomes 38 for a population of 1 million exposed to an 0.01 Gy gonadal dose of alpha radiation.

The BEIR V report also revised, markedly upward, the earlier BEIR III report (NAS/NRC, 1980) (and other) estimates of the degree to which irregularly inherited mutations contribute to human ill health. Accepting the estimates given in the BEIR V report, though emphasizing their extreme uncertainty, Addendum 1 made numerical estimates for three categories of irregularly inherited diseases—cancers, cardiovascular diseases, and a selected group of other diseases. These categories are presented in Table 4.2 of Addendum 1. Applying the RBE factor of 2.5 recommended in the BEIR IV Report to the Addendum 1 central estimates gives the results shown for alpha particle exposures in Table 4.2. We again emphasize, however, the extreme uncertainty of such numerical estimates, given the underlying uncertainties regarding the influence of genetic factors, and thus of mutation rates, on this class of human ill health.

Table 4.2 (Derived from Table 4.2, NUREG/CR-4214, Rev. 1, Addendum 1)

Genetic risk estimates for selected irregularly inherited diseases except for congenital anomalies for a population of 1 million persons exposed to a gonadal dose of 0.01 Gy of alpha radiation. Based on estimate of normal incidences given in BEIR V report (NAS/NRC, 1990); Addendum 1 (NRC, 1991), and the present analysis[a].

	Low-LET chronic Addendum 1			Alpha radiation (this report)	
Type of disorder	Normal incidence[b]	First generation	All generations	First generation	All generations
Cancer	144,000	7 [c]	190	18 [c]	475
Cardiovascular	288,000	18	375	45	940
Selected other	144,000	9	190	23	475
TOTALS[d]	576,000	35	760	85	1,900

[a] We emphasize here, as well as in the text, the extremely tenuous nature of these numerical estimates in light of the very large uncertainties involves.

[b] Assumes a population of 10^6 persons of all ages will produce 480,000 offspring per generation (30 years).

[c] Estimates based on assumption there are between 50 and 100 "tumor suppressor" genes that might be mutated (see Addendum 1).

[d] Totals rounded to avoid impression of great precision.

4.3.6 Periimplantation Wastage

Estimates of periimplantation wastage were made in NUREG/CR-4214 (NRC, 1989a). These early losses are believed to be caused mainly by chromosomal abnormalities, one quarter of which may be caused by unbalanced translocations and the remainder by aneuploidy (see NRC, 1989a). Adopting the BEIR IV recommendations of an RBE of 2.5 for mutations (which are used here for aneuploidy) and 15 for chromosomal aberrations, the combined RBE factor for periimplantation wastage induced by gonadal exposure to alpha radiation becomes 5.6 [(.25 x 15)+(0.75 x 2.5) = 5.63]. Using this RBE factor, the Addendum 1 central estimates of 230 in the first generation and 240 over all generations become 1295 in the first generation and 1351 over all future generations for a population of 1 million persons exposed to a gonadal alpha radiation dose of 0.01 Gy.

4.4 Summary

The RBE factors recommended in the BEIR IV report (NAS/NRC, 1988) have been used to convert estimates of genetic effects from exposure to low-dose-rate, low-LET radiation given in Addendum 1 (NRC, 1991) to estimates for internally deposited, alpha-emitting radionuclides. Using an RBE of 2.5 for all mutations and 15 for unbalanced translocations, the numbers of genetic effects that might occur as a consequence of a nuclear power plant accident were estimated for the various classes of effects. These results are tabulated in Tables 4.1 and 4.2 to facilitate inclusion into the NUREG/CR-4214 health effects models (NRC, 1989a). Specifically, it is recommended that the alpha and low-LET, radiation-associated risks be evaluated separately, then added.

REFERENCES

Abrahamson, S. and Wolff, S. (1976) Reanalysis of Radiation-Induced Specific Locus Mutations in the Mouse, *Nature 264*:715-719.

Abrahamson, S., Meyer, H.V., and DeJongh, C. (1981) The Shapes of Radiation Dose-Mutation Response Curves in Drosophila: Mechanisms and Implications. In: *Measurements of Risks*, G.G. Berg and H.D. Maillie, eds., pp. 477-492, Plenum Publishing Co., New York.

Aldrich, D.C. and Sprung, J.L. (1982) *Technical Guidance for Siting Criteria Development*, NUREG/CR-2239, SAND81-1549, Sandia National Laboratories.

Alpert, D.J., Chanin, D.I., and Ritchie, L.T. (1986) *Relative Importance of Individual Elements to Reactor Accident Consequences Assuming Equal Release Fractions*, NUREG/CR-4467, SAND85-2575, Sandia National Laboratories.

Bair, W.J., Richmond, C.R., and Wachholz, B.W. (1974) *A Radiobiological Assessment of the Spatial Distribution of Radiation Dose from Inhaled Plutonium*, WASH 1320, U.S. Atomic Energy Commission, Washington, DC.

Baverstock, K.F. and Papworth, D.G. (1989) The UK Radium Lumenizer Survey. In: *Risks from Radium and Thorotrast*, Workshop Proceedings, D.M. Taylor, C.W. Mays, G.B. Gerber, and R.G. Thomas, eds. pp. 72-76, BIR Report 21, British Institute of Radiology, London.

BIR (1989) D.M. Taylor, C.W. Mays, G.B. Gerber and R.G. Thomas, eds. *Risk from Radium and Thorotrast*, Workshop Proceedings, BIR Report 21, British Institute of Radiology, London.

Boecker, B.B., Hahn, F.F., Muggenburg, B.A., Guilmette, R.A., Griffith, W.C., and McClellan, R.O. (1988) The Relative Effectiveness of Inhaled Alpha and Beta Emitting Radionuclides in Producing Lung Cancer. In: *Radiation Protection Practice, Proceedings of the Seventh International Congress of IRPA*, Sydney, Australia, pp. 1059-1062, Vol. II, Pergamon Press, Sydney, Australia.

Brooks, A.L., Mewhinney, J.A., and McClellan, R.O. (1972) The *In Vivo* Cytogenetic Effects of ^{252}Cf on Liver and Bone Marrow of the Chinese Hamster, *Health Phys.* 22:701-706.

Brooks, A.L. (1975) Chromosome Damage in Liver Cells from Low Dose Rate Alpha, Beta, and Gamma Irradiation: Derivation of RBE, *Science 190:*1090-1092.

Cardozo, B.L., Zoetelief, H., van Bekkum, D.W., Zurcher, C., and Hagenbeek, A. (1985) Lung Damage Following Bone Marrow Transplantation. I. The Contribution of Irradiation, *Int. J. Radiat. Oncol. Biol. Phys. 11*:907-914.

Chemelevsky, D., Kellerer, A.M., Spiess, H. and Mays, C.W. (1986) A Proportional Hazards Analysis of Bone Sarcoma Rats in German Radium-224 Patients. In *The Radiobiology of Radium and Thorotrast*, W. Gössner, G.B. Gerber, V. Hagen and A. Luz, eds., Urban & Schwartzenberg, Munich.

Cuddihy, R.G. (1982) Risks of Radiation-Induced Lung Cancer. In *Critical Issues in Setting Radiation Dose Limits*, Proceedings No. 3, pp. 133-152, NCRP, Bethesda, MD.

Dagle, G.E., Park, J.F., Weller, R.E., Ragan, H.A., and Stevens, D.L. (1986) Pathology Associated with Inhaled Plutonium in Beagles. In: *Life-Span Radiation Effects Studies in Animals: What Can They Tell Us?*, R.C. Thompson and J.A. Mahaffey, eds., pp. 471-476, CONF-830951, National Technical Information Service, Springfield, VA.

Dagle, G.E., Park, J.F., Gilbert, E.S., and Weller, R.E. (1989) Risk Estimates for Lung Tumors from Inhaled $^{239}PuO_2$, $^{238}PuO_2$, and $^{239}Pu(NO_3)_3$ in Beagle Dogs, *Radiat. Prot. Dosim. 26*:173-176.

Diel, J.H. (1978) Local Dose to Lung Tissue from Inhaled $^{238}PuO_2$ Particles, *Radiat. Res. 75*:348-372.

Doenecke, F. and Belt, J.H. (1931) Über tödliche Lungenfibrose bei gewerblicher Radiumschädigung *Frankfurt. Z. Path. 42*:161-170. (referenced in Spencer, H. (1985) *Pathology of the Lung*, Pergamon Press, Oxford, UK).

Dolphin, G.W., Smith, H., Popplewell, D.S., Stather, J.W., Adams, N., Spoor, N.L., Brightwell, J. and Bulmann, R.A. (1974) *Radiobiological Problem in the Protection of Persons Exposed to Plutonium*, Report NRPB-R29, National Radiological Protection Board, Harwell, England.

Down, J.D. and Steel, G.G. (1983) The Expression of Early and Late Damage After Thoracic Irradiation: A Comparison Between CBA and C57B1 Mice, *Radiat. Res. 96*:603-610.

DuMouchel, D. and Groër, P.G. (1989) A Bayesian Methodology for Scaling Radiation Studies from Animals to Man, *Health Phys. 57 Suppl. 1*:411-418.

Dunjic, A., Maisin, J., Maldague, P., and Maisin, H. (1960) Incidence of Mortality and Dose-Response Relationships Following Partial-Body X-Irradiation of the Rat, *Radiat. Res. 12*:155-166.

Evans, R.D., Keane, A.T., and Shanahan, M.M. (1972) Radiogenic Effects in Man of Long-Term Skeletal Alpha-Irradiation. In: *Radiobiology of Plutonium*, B. J. Stover and W. S. S. Jee, eds., pp. 431-468, The J. W. Press, Salt Lake City.

Gilbert, E.S., Fry, S.A., Wiggs, L.D., Voelz, G.L., Cragle, D.L., and Peterson, G.R. (1989a) Analyses of Combined Mortality Data on Workers at the Hanford Site, Oak Ridge National Laboratory, and Rocky Flats Nuclear Weapons Plant, *Radiat. Res. 120*:19-35.

Gilbert, E.S., Park, J.F., and Buschbom, R.L. (1989b) Time-Related Factors in the Study of Risks in Animals and Humans, *Health Phys. 57, Suppl. 1*:379-385.

Gillett, N.A., Muggenburg, B.A., Mewhinney, J.A., Hahn, F.F., Seiler, F.F., Boecker, B.B., and McClellan, R.O. (1988) Primary Liver Tumors in Beagle Dogs Exposed by Inhalation to Aerosols of Plutonium-238 Dioxide, *Am. J. Pathol. 133*:265-275.

Gössner, W., Gerber, G.B., Hagen, U., and Luz, A., eds. (1986) *The Radiobiology of Radium and Thorotrast*, Urban & Schwarzenberg, Munich.

Hahn, F.F., Griffith, W.C., Boecker, B.B., Muggenburg, B.A., and Lundgren, D.L. (1992) Comparison of the Effects of Inhaled $^{239}PuO_2$ and β-Emitting Radionuclides on the Incidence of Lung Carcinomas in Laboratory Animals. In: *Proceedings of the Eighth International Congress of IRPA*, Montreal, Canada, pp. 916-919.

Humphreys, E.R., Loutit, J.F., Major, I.R., and Stones, V.A. (1985) The Induction by ^{224}Ra of Myeloid Leukemia and Osteosarcoma in Male CBA Mice, *Int. J. Radiat. Biol. 47*:239-247.

Humphreys, E.R., Loutit, J.F., and Stones, V.A. (1987) The Induction, by ^{239}Pu, of Myeloid Leukemia and Osteosarcoma in Female CBA Mice, *Int. J. Radiat. Biol. 51*:331-339.

Humphreys, E.R., Major, J.R., and Stones, V.A. (1989) Myeloid Leukemia/Osteosarcoma Ratio in CBA/H Mice Given Radium 224. In: *Risks from Radium and Thorotrast*, Workshop Proceedings, D.M. Taylor, C.W. Mays, G.B. Gerber and R.G. Thomas, eds., pp. 36-39, BIR Report 21, British Institute of Radiology, London.

ICRP (1963) Report of the RBE Committee to the International Commission on Radiological Protection and the International Commission on Radiation Units and Measurements, *Health Phys. 9*:357-386.

ICRP (1979) International Commission on Radiological Protection, *Limits for Intakes of Radionuclides by Workers*, ICRP Publication 30, Pergamon Press, Oxford, UK.

ICRP (1980) International Commission on Radiological Protection, *Biological Effects of Inhaled Radionuclides*, ICRP Publication 31, Pergamon Press, Oxford, UK.

ICRP (1987) International Commission on Radiological Protection, *Lung Cancer Risk from Indoor Exposure to Radon Daughters*, ICRP Publication 50, Pergamon Press, Oxford, UK.

ICRP (1990) International Commission on Radiological Protection, *RBE for Deterministic Effects*, ICRP Publication 58, Pergamon Press, Oxford, UK.

ICRP (1991) International Commission on Radiological Protection, *1990 Recommendations of the International Commission on Radiological Protection*, ICRP Publication 60, Pergamon Press, Oxford, UK.

Jow, H.-N. and Sprung, J.L. (1990) Reactor Accident Consequence Analysis Code (MACCS). In: *Proceedings of the Health Physics Society 23rd Midyear Topical Symposium, Risk: Perception, Assessment, Management and Communication, February 5-8, 1990, Atlantic City, NJ*, pp. 87-96.

Kurohara, S.S. and Casarett, G.W. (1972) Effects of Single Thoracic X-ray Exposure in Rats, *Radiat. Res. 52*:263-290.

Lundgren, D.L., Hahn, F.F., Diel, J.H. and Snipes, M.B. (1992a) Repeated Inhalation Exposure of Rats to Aerosols of $^{144}CeO_2$ I. Lung, Liver, and Skeletal Dosimetry, *Radiat. Res. 132*:312-314.

Lundgren, D.L., Hahn, F.F., and Diel, J.H. (1992b) Repeated Inhalation Exposure of Rats to Aerosols of $^{144}CeO_2$ II. Effects on Survival and Lung, Liver, and Skeletal Neoplasms, *Radiat. Res. 132*:325-333.

Masse, R. and Cross, F.T. (1989) Risk Considerations Related to Lung Modeling, *Health Phys. 57, Suppl. 1*:283-289.

Mays, C.W., Taylor, G.N., Jee, W.S.S., and Dougherty, T.S. (1970) Speculated Risk to Bone and Liver from ^{239}Pu, *Health Phys. 19*:601-610.

Mays, C.W. and Finkel, M.P. (1980) RBE of α-Particles vs. β-Particles in Bone Sarcoma Induction. In *Proceedings of the Fifth International Congress of IRPA*, Jerusalem, Israel, pp. 401-405.

Mays, C.W. (1982) Risk Estimates for Liver. In *Critical Issues in Setting Radiation Dose Limits*, Proceedings No. 3, pp. 182-196, NCRP, Bethesda, MD.

Mays, C.W. and Spiess, H. (1984) Bone Sarcomas in Patients Given Radium-224. In: *Radiation Carcinogenesis. Epidemiology and Biological Significance*, J.B. Boice, and J.F. Fraumeni, eds., pp. 241-252, Raven, New York.

Mays, C.W., Spiess, H., Chmelevsky, D. and Kellerer, A. (1986) Bone Sarcoma Cumulative Tumor Rates in Patients Injected with Radium-224. In:*The Radiobiology of Radium and Thorotrast*, W. Gössner, G.B. Gerber, U. Hagen and A. Luz, eds.) pp. 27-31, Urban and Schwarzenberg, Munich.

Mays, C.W., Lloyd, R.D, Taylor, G.N., and Wrenn, M.E. (1987) Cancer Incidence and Lifespan vs. α-Particle Dose in Beagles, *Health Phys. 52*:617-624.

Medical Research Council (1975) *The Toxicity of Plutonium*, Her Majesty's Stationery Office, London.

Muggenburg, B.A., Boecker, B.B., Hahn, F.F., Griffith, W.C. and McClellan, R.O. (1986) The Risk of Liver Tumors in Dogs and Man from Radioactive Aerosols. In: *Life-Span Radiation Effects Studies in Animals: What Can They tell Us?*, R. C. Thompson and J. A. Mahaffey, eds., pp. 556-563, CONF-830951, OSTI, Oak Ridge, TN.

Muggenburg, B.A., Wolff, R.K., Mauderly, J.L., Plaggmier, M. M., Hahn, F.F., Guilmette, R.A. and Gerlach, R.F. (1988) Cardiopulmonary Function of Dogs with Plutonium-Induced Chronic Lung Injury. *Radiat. Res. 115*:314-324.

NAS/NRC (1976) National Academy of Sciences/National Research Council, *Health Effects of Alpha-Emitting Particles in the Respiratory Tract*, Report of the Ad Hoc Committee on "Hot Particles," EPA 520/4-76-013, U.S. Environmental Protection Agency, Washington, D.C.

NAS/NRC (1980) National Academy of Sciences/National Research Council, *The Effects on Populations of Exposures to Low Levels of Ionizing Radiation, BEIR III*, Committee on the Biological Effects of Ionizing Radiations, National Academy Press, Washington, DC.

NAS/NRC (1988) National Academy of Sciences/National Research Council, *Health Risks of Radon and Other Internally Deposited Alpha-Emitters, BEIR IV*, Committee on the Biological Effects of Ionizing Radiations, National Academy Press, Washington, DC.

NAS/NRC (1990) National Academy of Sciences/National Research Council, *Health Effects of Exposure to Low Levels of Ionizing Radiation, BEIR V*, Committee on the Biological Effects of Ionizing Radiations, National Academy Press, Washington, DC.

NCRP (1975) National Council on Radiation Protection and Measurements, *Alpha-Emitting Particles in Lungs*, Report 46, NCRP, Bethesda, MD.

NCRP (1984) National Council on Radiation Protection and Measurements, *Evaluation of Occupational and Environmental Expsoures to Radon and Radon Daughters in the United States*, Report 78, NCRP, Bethesda, MD.

NCRP (1987) National Council on Radiation Protection and Measurements, *Recommendations on Limits for Exposure to Ionizing Radiation*, Report 91, NCRP, Bethesda, MD.

NCRP (1990) National Council on Radiation Protection and Measurements, *The Relative Biological Effectiveness of Radiation of Different Quality*, Report 104, NCRP, Bethesda, MD.

Neary, G.J., Savage, J.R.K., and Evans, H.J. (1961) *Effects of Ionizing Radiation on Seeds*, International Atomic Energy Agency, Vienna, Austria.

Nenot, J.C. and Stather, J.W. (1979) *The Toxicity of Plutonium, Americium and Curium*, Commission of the European Communities Publication, Pergamon Press, Oxford, UK.

NRC (1975) *Reactor Safety Study: An Assessment of Accident Risks in the U.S. Commercial Nuclear Power Plants, Appendix VI. Calculaiton of Reactor Accident Consequences*, Report NUREG-75/014, U.S. Nuclear Regulatory Commission, Washington, DC.

NRC (1985) *Health Effects Model for Nuclear Power Plant Accident Consequence Analysis. Part II: Scientific Basis for Health Effects Models*, Report NUREG/CR-4214, U.S. Nuclear Regulatory Commission, Washington, DC.

NRC (1987) *Experimental Studies of the Early Effects of Inhaled Beta-Emitting Radionuclides for Nuclear Accident Risk Assessment*, Report NUREG/CR-5025, U.S. Nuclear Regulatory Commission, Washington, DC.

NRC (1988a) *Inhaled $^{239}PuO_2$ and/or Total-Body Gamma Radiation: Early Mortality and Morbidity in Rats and Dogs*, Report NUREG/CR-5198, U.S. Nuclear Regulatory Commission, Washington, DC.

NRC (1988b) *Early and Continuing Effects of Combined Alpha and Beta Irradiation of the Lung*, Report NUREG/CR-5067, U.S. Nuclear Regulatory Commission, Washington, DC.

NRC (1989a) *Health Effects Models for Nuclear Power Plant Accident Consequence Analysis. Low LET Radiation. Part II: Scientific Bases for Health Effects Models*, Report NUREG/CR-4214 Rev. 1, Part II, U.S. Nuclear Regulatory Commission, Washington, DC.

NRC (1989b) *Models for Pulmonary Lethality and Morbidity After Irradiation From Internal and External Sources*, Report NUREG/CR-5351, U.S. Nuclear Regulatory Commission, Washington, DC.

NRC (1989c) *Inhaled ^{147}Pm and/or Total-Body Gamma Radiation: Mortality and Morbidity in Rats*, Report NUREG/CR-5353, U.S. Nuclear Regulatory Commission, Washington, DC.

NRC (1990a) *Health Effects Models for Nuclear Power Plant Accident Consequence Analysis. Low LET Radiation. Part I: Introduction, Integration and Summary*, Report NUREG/CR-4214 Rev. 1, Part I, U.S. Nuclear Regulatory Commission, Washington, DC.

NRC (1990b) *MELCORE Accident Consequence Code System (MACCS)*, Report NUREG/CR-4691, SAND86-1562, Vol. 1, U.S. Nuclear Regulatory Commission, Washington, DC.

NRC (1991) *Health Effects Models for Nuclear Power Plant Accident Consequence Analysis. Modifications of Models Restulting from Recent Reports on Health Effects of Ionizing Radiation. Low LET Radiation. Part II: Scientific Bases for Health Effects Models*, Report NUREG/CR-4214 Rev. 1, Part II, Addendum 1, U.S. Nuclear Regulatory Commission, Washington, DC.

Priest, N.D. (1989) Alpha-Emitters in the Skeleton: An Evaluation of the Risk of Leukemia Following Intakes of Plutonium 239. In: *Risks from Radium and Thorotrast*, Workshop Proceedings, D.M. Taylor, C.W. Mays, G.B. Gerber and R.G. Thomas, eds., pp. 36-39, BIR Report 21, British Institute of Radiology, London.

Puskin, J.S., Nelson, N.S. and Nelson, C.B. (1992) Bone Cancer Risk Estimates. *Health Phys. 63*:579-580.

Ragan, H.A., Buschbom, R.L., Park, J.F., Dagle, G.E. and Weller, R.E. (1986) Hematologic Effects of Inhaled Plutonium in Beagles. In: *Life-Span Radiation Effects Studies in Animals: What Can They Tell Us?*, R.C. Thompson and J.A. Mahaffey, eds., pp. 477-486, CONF-830951, National Technical Information Service, Springfield, VA.

Rajewsky, B. (1939) Researches in the Problem of Radium Poisoning and the Tolerance Dose of Radium, *Radiology 32*:57-62.

RERF (1987) Radiation Effects Research Foundation. *U.S.-Japan Joint Reassessment of Atomic Bomb Radiation Dosimetry in Hiroshima and Nagasaki. Final Report*, RERF, Hiroshima, Japan.

Rosenthal, M.W., Moretti, E., Russell, J.J. and Lindenbaum, A. (1972) Marrow Deposition and Distribution of Monomeric and Polymeric ^{239}Pu in the Mouse, Estimated by the Use of ^{59}Fe, *Health Phys. 22*:743-748.

Ross, D.M. (1968) A Statistical Summary of USAEC Licensees Internal Exposure Experience,. In: *Diagnosis and Treatment of Deposited Radionuclides*, H.A. Kornberg, and W.C. Norwood, eds., pp. 437-444, Excerpta Medica Foundation, Amsterdam.

Rowland, R.E., Stehney, A.F. and Lucas, H.F., Jr. (1978) Dose-Response Relationships for Female Radium Dial Workers, *Radiat. Res. 76*: 368-383.

Sanders, C.L. and Lauhala, K.E. (1992) Low-Level $^{239}PuO_2$ Life-Span Studies. In: *Pacific Northwest Laboratory Annual Report for 1991 to the DOE Office of Energy Research, Part I: Biomedical Sciences*, pp. 27-34, PNL-8000, Pt. 1.

Scott, B.R., Hahn, F.F., Guilmette, R.A., Muggenburg, B.A., Snipes, M.B., Boecker, B.B., and McClellan, R.O. (1986) Use of Studies with Laboratory Animals to Assess the Potential Early Health Effects of Combined Internal Alpha and Beta Irradiation. In: *Life-Span Radiation Effects Studies in Animals: What Can They Tell Us?*, R.C. Thompson and J.A. Mahaffey, eds., pp. 578-591, CONF-830951, National Technical Information Service, Springfield, VA.

Scott, B.R., Hahn, F.F., McClellan, R.O., and Seiler, F.A. (1988) Risk Estimators for Radiation-Induced Bone Marrow Syndrome Lethality in Humans, *Risk Anal. 8*:393-402.

Scott, B.R. (1988) A Radiation Protection Approach to Assessing Population Risk for Threshold-Type Radiation Effects, *Health Phys. 55*:463-470.

Scott, B.R. (1989) Probabilistic Models for Early and Continuing Radiobiological Effects of Nuclear Power Plant Accidents. In: *Proceedings for PSA '89 International Topical Meeting, Probability, Reliability, and Safety Assessment*, April 2-7, 1989, Pittsburgh, PA, pp. 732-737.

Scott, B.R. and Dillehay, L.E. (1990) A Model for Hematopoietic Death in Man From Irradiation of Bone Marrow During Radioimmunotherapy, *Br. J. Radiol. 63*:862-880.

Scott, B.R., Hahn, F.F., Snipes, M.B., Newton, G.J., Eidson, A.F., Mauderly, J.L., and Boecker, B.B. (1990) Predicted and Observed Early Effects of Combined Alpha and Beta Irradiation of the Lung, *Health Phys. 59*:791-805.

Spencer, H. (1973) *Pathology of the Lung*, Pergamon Press, Oxford, UK.

Spiers, F.W., Lucas, H.F., Rundo, J., and Anast, G.A. (1983) Leukemia Incidence in the U.S. Dial Workers, *Health Phys. 44, Suppl. 1*:65-72.

Spiess, M., Mayes, C.W., and Chmelevsky, D. (1989) Malignancies in Patients Injected with Radium 224. In: *Risk From Radium and Thorotrast*, Workshop Proceedings, D.M. Taylor, C.W. Mays, G.B. Gerber, and R.G. Thomas, eds., pp. 7-11, BIR Report 21, British Institute of Radiology, London.

Stannard, J.N. (1988) *Radioactivity and Health: A History*. R.W. Baalman, Jr., ed., DOE/RL/01830-T59 (DE88013791), National Technical Information Service, Springfield, VA.

Stebbings, J.H., Lucas, H.F., and Stehney, A.F. (1984) Mortality from Cancers of Major Sites in Female Radium Dial Workers, *Am. J. Indust. Med. 5*:455-459.

Stevens, W., Stover, B.J., Atherton, D.R. and Bruenger, F.W. (1975) Distribution and Excretion of Three Chemical Species of ^{239}Pu(IV) in the Beagle, *Health Phys. 28*:387-394.

Straume, T., Ebert, S.D., Woolson, W.A., Finkel, R.C., Kubick, P.W., Gove, H.E., Sharma, P. and Hoshi, M. (1992) Neutron Discrepancies in the DS86 Hiroshima Dosimetry System, *Health Phys. 63*:421-426.

Taube, M. (1964) *Plutonium*, Lepa, E. and Nanowski, Z, trans., Macmillan, New York.

Taylor, G.N., Lloyd, R.D., Mays, C.W., Angus, W., Miller, S.C., Shabestari, L. and Hahn, F.F. (1991) *Health Phys. 61*:337-347.

Taylor, G.N., Mays, C.W., Lloyd, R.D., Jones, C.W.,, Rojas, J., Wrenn, M.E., Ayoroa, G., Kaul, A. and Riedel, W. (1986) Liver Cancer Induction by ^{241}Am and Thorotrast in Deer Mice and Grasshopper Mice. In: *The Radiobiology of Radium and Thorotrast*, W. Gössner, G.B. Gerber, U. Hagen and A. Luz, eds.) pp. 172-177, Urban and Schwarzenberg, Munich.

Thompson, R.C. and Mahaffey, J.A. (eds.) (1986) *Life-Span Radiation Effects Studies in Animals: What Can They Tell Us?* National Technical Information Service, Springfield, VA, US DOE Report CONF-830951.

Thompson, R.C. (1989) *Life-Span Effects of Ionizing Radiation in the Beagle Dog, A Summary Account of Four Decades of Research Funded by the U.S. Department of Energy and its Predecessor Agencies*. USDOE Report, PNL-6822, Pacific Northwest Laboratories, Richland, WA.

Tietjen, G.L. (1987) Plutonium and Lung Cancer, *Health Phys. 52*:625-628.

UNSCEAR (1986) *Genetic and Somatic Effects of Ionizing Radiation*, United Nations Scientific Committee on the Effects of Atomic Radiation Report to the General Assembly, with Annexes, United Nations, New York.

UNSCEAR (1988) *Sources, Effects and Risks of Ionizing Radiation*, United Nations Scientific Committee on the Effects of Atomic Radiation Report to the General Assembly, with Annexes, United Nations, New York.

USSR (1986) *The Accident at the Chernobyl Nuclear Power Plant and Its Consequences*, USSR State Committee on the Utilization of Atomic Energy, information compiled for the IAEA Experts' Meeting, August 25-29, 1986, Vienna, Part I. General Material, Annexes 1-7.

Voelz, G.L., Wilkinson, G.W., Healy, J.W., McInroy, J.F., and Tietjen, G.L. (1983) Mortality Study of Los Alamos Workers with Higher Exposures to Plutonium. In *Epidemiology Applied to Health Physics, Proceedings of Health Physics Society Sixteenth Midyear Topical Meeting*, Albuquerque, NM, National Technical Information Service, Springfield, VA, Report CONF-83010, pp. 318-327.

Voelz, G.L. and Lawrence, J.N.P. (1991) A 42-y Medical Follow-Up of Manhattan Project Plutonium Workers, *Health Phys. 61*:181-190.

WHO (1982) World Health Organization, *Nuclear Power Health Implications of Transuranium Elements*, WHO Regional Publications, European Series No. 11, World Health Organization Regional Office for Europe, Copenhagen.

Wilkinson, G.S., Tietjen, G.L., Wiggs, L.D., Galke, W.A., Acquavella, J.F., Reyes, M., Voelz, G.L., and Waxweiler, R.J. (1987) Mortality Among Plutonium and Other Radiation Workers at a Plutonium Weapons Facility, *Am. J. Epidemiol. 125*:231-250.

Yaniv, S.S. and Scott, B.R. (1991) Revised Nonstochastic Health Effects Models. In: *Proceedings of the CEC Seminar on Methods and Codes for Assessing the Consequences of Nuclear Accidents*, May 7-11, 1990, Athens, pp. 773-791, Commission of the European Communities, Luxemborg, Publication EUR13013.

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11. ABSTRACT *(200 words or less)*

Several studies designed to identify and quantify the potential health effects of accidental releases of radionuclides from nuclear power plants have been sponsored by the Nuclear Regulatory Commission. Report NUREG/CR-4214, Rev. 1, Part II (NRC, 1989a) describes in detail the most recent health effects models that have evolved from these efforts. Since the Part II report was published in 1989, two addenda to that report have been prepared to 1) incorporate other scientific information related to low-LET health effects models and 2) extend the models to consider the possible health consequences of including alpha-emitting actinide radionuclides in the exposure source term. The first addendum was published as NUREG/CR-4214, Rev. 1, Part II, Addendum 1 (NRC, 1991). This report, the second addendum to the Part II report, extends the health effects models to consider chronic irradiation from alpha-emitting radionuclides as well as low-LET sources. Consistent with the organization of past reports, this report has three main sections that address early-occurring and continuing effects, late somatic effects, and genetic effects. These results should be used with the basic NUREG/CR-4214 report and Addendum 1 to obtain current views on potential health effects models for radionuclides released accidentally from nuclear power plants.

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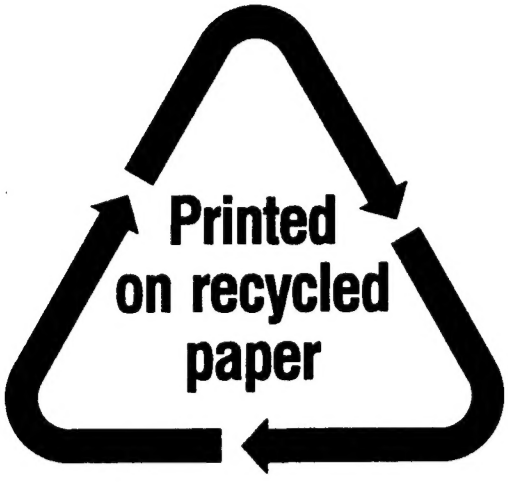

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